Introduction to Continuous Kidney Replacement Therapy

CKRT | CRRT

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This book provides a concise practical introduction to continuous kidney replacement therapy (CKRT, also termed CRRT), combining basic principles, clinical applications and a review of the relevant evidence.

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Scientific and Historical Overview

Origins and Historical Development

Continuous kidney replacement therapy initially developed from research into ultrafiltration and convective transport. In 1967, Henderson and colleagues published a description of blood purification by ultrafiltration with fluid replacement, an early contribution to the development of haemofiltration techniques [1].

In 1974, Silverstein and colleagues published a study entitled “Treatment of severe fluid overload by ultrafiltration” [2]. The paper published by Kramer and colleagues in 1977 provides an early clinical description of continuous arteriovenous haemofiltration (CAVH); the work was conducted in Göttingen, in what was then West Germany. A capillary haemofilter was used, and the arteriovenous pressure gradient drove blood through the circuit without a blood pump. The report focused on fluid removal in patients with diuretic-resistant fluid overload and described a blood flow of approximately 100 mL/min, an ultrafiltration rate of 200–600 mL/h, and the possibility of continuing to use the filter for up to 48 hours [3].

In 1980, Kramer and colleagues described their experience in anuric intensive care patients and concluded that CAVH allowed control of fluid balance in patients who had not responded to diuretics. They also reported its use in managing uraemia and hypernatraemia [4].

CAVH relied on the patient’s arterial pressure through an arterial access. Historical reviews state that limited toxin removal in highly catabolic states and problems with arterial access prompted the development of venovenous techniques driven by a blood pump.

Pump-driven CVVH techniques emerged in the mid-1980s and subsequently became more widespread as double-lumen venous catheters and pumping systems became available [5,6,10]. Diffusion was added to convection through the development of continuous arteriovenous haemodialysis (CAVHD); Geronemus and Schneider’s description of this technique was published in 1984.

As circuits moved to venovenous access, the modalities now known as CVVH, CVVHD and CVVHDF took shape. Each name indicates the predominant or employed transport component: convection in CVVH, diffusion in CVVHD, and their combination in CVVHDF [5,7].

Definition of Continuous Kidney Replacement Therapy:

This book uses the term continuous kidney replacement therapy (CKRT). The term continuous renal replacement therapy (CRRT) is also widely used in the literature.

The word “continuous” should not be understood to mean that treatment is never interrupted; the term describes a prolonged treatment modality compared with intermittent dialysis sessions, and the treatment time actually delivered may be affected by clinical or technical interruptions [5,8].

For terminology describing kidney function and disease, KDIGO recommends using “kidney” instead of “renal” and lists kidney replacement therapy (KRT) as the preferred term over renal replacement therapy (RRT). CKRT is therefore used here, while acknowledging that CRRT remains common in earlier publications and guidelines [8].

Treatment Modality Selection and What the Evidence Establishes

The 2012 KDIGO guidelines recommend using continuous and intermittent therapies as complementary options in acute kidney injury and suggest CKRT as an alternative to standard intermittent therapy in haemodynamically unstable patients, as well as in those with acute brain injury, increased intracranial pressure or generalised cerebral oedema; both recommendations are graded 2B. The guidelines explain that gradual removal of fluid and solutes provides the physiological basis for preferring the continuous modality in these settings [7]. However, a recommendation about modality selection does not mean that trials have established superiority of CKRT in final outcomes. A meta-analysis of randomised trials comprising 30 trials and 3774 patients found no clear difference in mortality between CKRT and intermittent haemodialysis, and no clear difference in hypotension during treatment was established. The certainty of evidence for most comparisons was rated low to moderate. The analysis suggested a possible increase in kidney recovery with CKRT compared with intermittent dialysis, but the estimate was inconclusive.

It is therefore not appropriate to assert a consistent benefit in survival or kidney recovery [9]. Accordingly, modality selection remains dependent on the clinical condition, the treatment goal and the ability to tolerate the rate of fluid removal and changes in solute concentrations, as well as the unit’s expertise and resources.

KDIGO acknowledges that no single modality is suitable for all patients with acute kidney injury [7].

Clinical Applications and Practical Limits

In acute brain injury, increased intracranial pressure or generalised cerebral oedema, KDIGO suggests CKRT as an alternative to intermittent therapy.

The guidelines state that rapid changes in blood pressure or solute concentrations during intermittent therapy may affect cerebral perfusion pressure or increase oedema and intracranial pressure. This rationale was based on observational data and clinical reports in addition to physiological considerations [7]. It is supported by the fact that urea is distributed throughout total body water but crosses the blood–brain barrier only slowly. Consequently, excessively rapid removal of urea from the circulation using intermittent forms of haemodialysis therapy (IHD) may promote movement of plasma water into the brain. The so-called reverse urea effect can cause or aggravate increased intracranial pressure, with potentially severe neurological consequences.

Severe liver failure is also associated with cerebral oedema and increased intracranial pressure; where these complications are present, CKRT may therefore be preferred. The cited KDIGO recommendation does not list liver failure alone as an independent indication for preferring CKRT. In patients with acute kidney injury and liver failure or lactic acidosis, KDIGO suggests bicarbonate rather than lactate in the dialysate or replacement fluid (conditional recommendation, grade 2B). This recommendation concerns fluid composition and does not by itself establish superiority of CKRT over other modalities [7].

The continuous modality can provide continuous control of fluid balance in an oliguric or anuric patient receiving therapeutic or nutritional fluids, including total parenteral nutrition (TPN). Fluid control, alongside management of uraemia and certain electrolyte disorders, was among the applications documented in Kramer’s report on intensive care patients. However, this does not make CKRT the only option; the decision remains individualised according to the patient’s condition and the available resources [4,7].

Because fluid and solute removal during CKRT is gradual, it may not achieve the required speed of correction when rapid removal of a dialysable substance or correction of a life-threatening disturbance is clinically necessary. KDIGO presents rapid removal of toxins and low-molecular-weight substances as a potential advantage of intermittent therapy. The modality should therefore be chosen according to the problem being treated, rather than assuming the absolute superiority of any one modality [7].

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Principles and Practical Prescription of CKRT

Continuous kidney replacement therapy (CKRT) is based on a prescription that combines solute removal, control of electrolytes and acid–base balance, and fluid management. These goals are not achieved merely by selecting a treatment modality; the outcome is influenced by vascular access, blood flow, solution composition, anticoagulation and actual circuit operating time. The prescription is therefore reviewed as the patient’s condition changes, and the prescribed dose is compared with the dose actually delivered.

The guideline recommendations presented here are based on the final 2012 KDIGO guideline, together with subsequent studies and updates. In October 2026, KDIGO described its 2026 update on acute kidney injury (AKI) and acute kidney disease (AKD) as a draft being prepared for publication after public consultation. The consultation period had ended on 11 May 2026. The draft is not treated here as a final guideline; the final 2012 guideline is identified separately. (2,8)

CKRT Principles and Modalities

Small solutes that are present at a higher concentration in the dialysis fluid (dialysate), such as bicarbonate, diffuse from the dialysate into the blood. On the other side of the membrane, dialysate flows in the direction opposite to blood flow (countercurrent), maintaining the concentration gradient needed to remove small solutes along the entire semipermeable membrane.

Almost all modern dialysers are high-flux dialysers and can remove larger substances than older low-flux dialysers could. Nevertheless, unlike haemofiltration, haemodialysis does not efficiently remove the larger middle molecules.

Ultrafiltration can also be performed during haemodialysis by applying a transmembrane pressure difference (TMP). However, unlike the large ultrafiltration volumes used in haemofiltration to achieve substantial solute removal, the ultrafiltration volumes used in haemodialysis are relatively small. They contribute little to small-solute removal and are used primarily to achieve net volume removal.

Overview of Modalities

Modalities are named according to the transport mechanism used, not solely according to treatment speed. CVVH relies primarily on convection, CVVHD primarily on diffusion, and CVVHDF combines both. SCUF focuses on ultrafiltration and fluid removal, while removal of a limited amount of solutes by convection remains possible [1,3].

Diffusion

Diffusion is the principal mechanism of solute removal in intermittent haemodialysis (IHD): solutes move across the membrane according to the concentration difference between blood and dialysate. This mechanism is particularly effective for removing small molecules, such as urea

and potassium. Countercurrent flow of blood and dialysate maintains the concentration difference along the filter, helping to sustain solute transport.

Convection

Convection is a term associated with ultrafiltration, which means the movement of water across the membrane under the effect of an effective pressure difference. The water carries with it solutes capable of crossing the membrane, and solute removal by this mechanism is termed convective filtration. The amount of solute removed depends on the ultrafiltrate volume and the solute’s sieving coefficient; it does not require a difference in solute concentration between the two sides of the membrane.

The hydrostatic pressure across the membrane, displayed by CKRT machines as TMP, differs from the effective filtration pressure. TMP can be approximated as the mean pressure on the blood side minus the pressure on the fluid side, taking into account differences in sensor locations and calculation methods between machines. Water movement is also influenced by the oncotic pressure difference generated by proteins.

Thus, the main driving force in diffusion is the difference in solute concentrations on the two sides of the membrane, whereas in the second mechanism (convection) it is hydrostatic pressure.

Note:

Although the term convection continues to be used, as is customary in the nephrology literature, to describe solute removal by haemofiltration, the physical transport of a substance by bulk fluid movement is technically more accurately termed advection rather than convection [9].

Modality	Predominant mechanism of solute removal	Dialysate	Replacement fluid
CVVH	Convection	No	Yes
CVVHD	Diffusion	Yes	No
CVVHDF	Convection and diffusion	Yes	Yes
SCUF	Ultrafiltration and limited solute removal by convection	No	No

Basic Terms and Equations

Before explaining the modalities and their details, the abbreviations must be understood:

Qb denotes the blood flow rate.

Qd denotes the dialysate flow rate.

Qrep denotes the replacement fluid flow rate.

QUF is the total ultrafiltrate flow rate leaving the blood compartment.

Qnet is the rate of net fluid removal from the patient.

SC is the sieving coefficient for solutes.

KUF is the filter's ultrafiltration coefficient.

TMP is the hydrostatic transmembrane pressure estimated by the machine from circuit pressures. Here, TMPeff denotes the effective filtration pressure after subtracting the opposing oncotic pressure difference; it need not equal the TMP displayed by a particular machine. [5]

As a simplified approximation, the ultrafiltration rate is related by the equation:

$QUF \approx KUF \times TMPeff$

Membrane properties and the pressure across it affect water flow; oncotic pressure resists and opposes filtration through the water-attracting force it generates.

Convective solute clearance can be approximated by the relationship Kconv ≈ QUF × SC.

SC is defined as the ratio of the solute concentration in the ultrafiltrate to its concentration in plasma. This is an approximate relationship; solute clearance does not always equal QUF, and performance is also influenced by predilution and by the properties of the solutes and the membrane [1,3,4].

In CVVHD, the ratio of the solute concentration in the outgoing dialysate to its concentration in plasma describes the degree of saturation of that fluid. This ratio is conceptually different from the sieving coefficient, although both may approach one for certain small solutes.

Clarification Regarding TMP:

If TMP is the hydrostatic pressure difference displayed by the machine, the oncotic pressure difference is considered separately. If, however, the symbol is defined as the effective filtration pressure after subtraction of oncotic pressure, this component must not be subtracted twice. This is a physiological and definitional note, which is explained in greater detail shortly [5,10].

1. Continuous Venovenous Hemofiltration (CVVH)

CVVH relies mainly on convection: water crosses the membrane because of an effective pressure difference and carries solutes with it. In a simplified model, the ultrafiltrate flow (Uf) is Uf = Kf × TMPeff, where Kf is the hydraulic permeability coefficient. The effective filtration pressure TMPeff is given by:

$$TMPeff = (Pb - Puf) - \pi$$

where:

Pb is the hydrostatic pressure in the blood.

Puf is the hydrostatic pressure in the ultrafiltrate.

Π is the plasma oncotic pressure.

The clearance of a substance by convection, Cx, is estimated using:

$$Cx = Quf \times S$$

and:

$$S = Cuf / Cp$$

where:

S is the sieving coefficient.

Cp is the concentration of the substance in plasma.

Cuf is the concentration of the same substance in the ultrafiltrate.

Water movement is accompanied by transport of solutes that can pass through the membrane, according to their sieving coefficient.

No dialysate is used in this modality; replacement fluid is used to replace most of the total ultrafiltrate [1,3].

In the simplified circuit balance, QUF = Qrep + Qnet. Thus, QUF is not equal to net fluid removal from the patient: the Qrep component returns to the circuit as replacement fluid, while the difference, Qnet, represents the intended net removal, with the remaining inputs and outputs accounted for in the clinical fluid balance [1,3].

Replacement fluid can be infused before the filter (predilution), after it (postdilution), or at both sites.

Predilution reduces the concentration of solutes entering the filter and therefore usually reduces clearance per unit of ultrafiltrate volume compared with postdilution. The infusion site also changes the concentration of blood within the filter. The actual dose must therefore be interpreted in relation to the site of replacement fluid administration [1,4].

KDIGO recommends an effluent volume of 20–25 mL/kg/h as the target dose for continuous kidney replacement therapy in acute kidney injury. The dose is calculated from the outgoing effluent volume, while net fluid removal is adjusted separately according to fluid balance. A higher rate may need to be prescribed to compensate for treatment interruptions, and solutes are removed at approximately the same rate [2].

Note:

For a freely filterable solute with a sieving coefficient (SC) of approximately 1 in an ideal well-mixed compartment, ultrafiltration removes water and solute in similar proportion, so ultrafiltration alone need not change its local plasma-water concentration. This high ultrafiltration rate would rapidly cause hypovolaemia without replacement fluid. Replacement fluid lowers the solute concentration by dilution, particularly when it contains none of that solute, as with urea. For incompletely filterable or protein-bound solutes, ultrafiltrate concentration can be lower than the corresponding total plasma concentration. Separately, redistribution between body compartments can limit total-body removal and affect serum concentrations over time.

A blood flow of 5–6 times the replacement-fluid flow is only a rough guide and does not by itself guarantee a filtration fraction below 20–25%. Calculate filtration fraction from the relevant plasma flow, hematocrit, total ultrafiltration, net fluid removal and predilution flows, using the device-specific definitions and protocol. Reducing excessive hemoconcentration helps limit filter clotting. [9,10]

Illustrative Example:

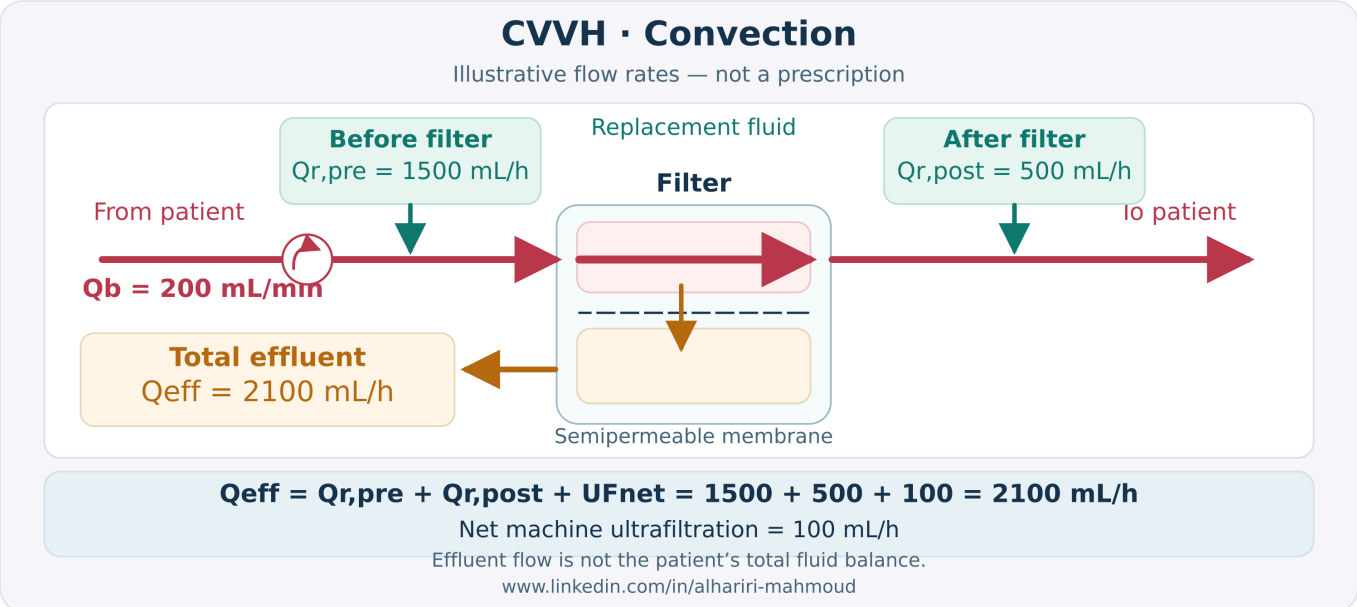
Flow values in the example:

Qb 200 mL/min

Qr 1500 mL/h before the filter and 500 mL/h after it.

UFnet is 100 mL/h.

Qef equals 2100 mL/h.



The dose in the preceding example is 2100 mL/h, equivalent to 30 mL/kg/h in a person weighing 70 kg. The blood flow is 200 mL/min, or 12,000 mL/h, approximately 6 times the replacement rate of 2000 mL/h.

2. Continuous Venovenous Hemodialysis (CVVHD)

CVVHD relies primarily on diffusion, in which solutes move across the membrane along the concentration gradient between blood and dialysate, from higher to lower concentration. Dialysate usually flows in the direction opposite to blood flow to maintain the concentration gradient along the filter.

Replacement fluid is not usually used; net fluid removal is achieved through an overall negative balance, meaning that the volume of fluid leaving exceeds the total volume of fluid entering the patient [1,3].

The magnitude of the diffusive solute transport rate, Sd, can be estimated for a simplified planar membrane using Fick's law:

$Sd = (Cg / Mt) \times D \times A$

where:

Cg is the concentration difference between the two sides of the membrane; Cg/Mt is the concentration gradient.

Mt is the membrane thickness.

D is the effective diffusion coefficient of the solute in the membrane.

T is the absolute temperature of the solution; its effect is already included in D and is not multiplied again.

A is the membrane surface area.

Cg is generally influenced by both:

Qd, the dialysate flow rate.

Qb, the blood flow rate.

However, because Qd is much lower than Qb, with typical Qd values of 5–80 mL/min versus Qb values of 100–200 mL/min, the dialysate usually becomes almost fully saturated with solutes during CVVHD.

Consequently, Qd becomes the rate-limiting factor for small-solute removal, whereas the influence of Qb is limited within the Qd and Qb ranges usually employed in CVVHD.

Note:

Fick's first law describes the diffusive solute flux along a homogeneous diffusion path in the following simplified expression; it is not a direct equation for calculating clearance in a dialysis machine: $J = -D\,dC/dx$

Assuming an approximately linear concentration gradient along a path of thickness δ, the rate of solute transfer can be approximated by the relationship: solute transfer rate ≈ (D × A / δ) × ΔC.

Here, J is the solute flux per unit area and time, D is the effective diffusion coefficient, A is the surface area available for diffusion, δ is the thickness of the diffusion path, and ΔC is the concentration difference between its ends. The negative sign in Fick's law indicates that diffusion proceeds towards lower concentration. This is an approximate relationship, because solute movement is also affected by the resistance of the blood and dialysate layers and the membrane, as well as by membrane structure and flow within it [5].

In some high-permeability filters, internal filtration and backfiltration occur along the fibres and may produce additional convective transport. Their magnitude, however, depends on filter design and circuit hydraulics. They should not be described as a guaranteed principal mechanism in every CVVHD treatment or automatically included in the prescribed convective dose [3,5].

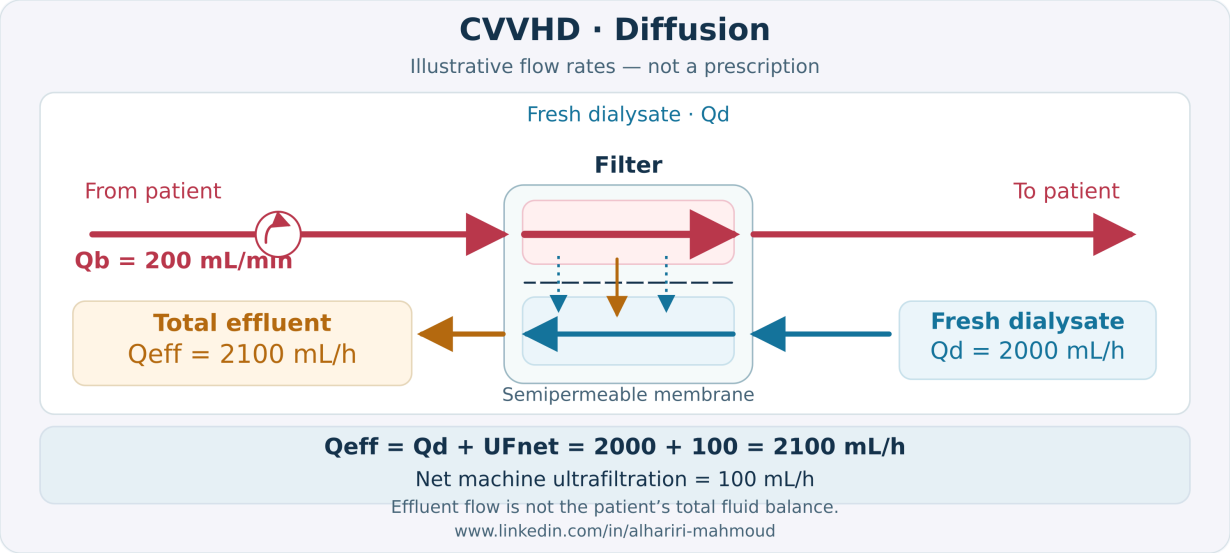
Illustrative Example:

Qb 200 mL/min

Qd 2000 mL/h

UFnet 100 mL/h

Qef equals 2100 mL/h.



Important Note:

In intermittent haemodialysis (IHD), high blood flow, approximately 300–500 mL/min, and high dialysate flow, 500–800 mL/min or approximately 30–48 L/h, are needed because the aim is substantial solute removal during a short session that usually lasts no more than a few hours. In continuous therapy (CRRT), removal is slow but continuous over 24–72 hours, so much lower flow rates are sufficient: blood flow of 100–200 mL/min and dialysate flow of approximately 1–2 L/h [9,10].

That is:

In IHD, dialysate flow is 1.5–2 times the blood flow.

In CKRT, however, blood flow is approximately 3 times or more the dialysate flow. This is because IHD aims to achieve maximal clearance and removal of toxins and solutes, whereas CRRT aims to provide continuous clearance with haemodynamic stability. IHD therefore depends more on high Qb and Qd, while the CRRT dose depends primarily on the total effluent dose.

3. Continuous Venovenous Hemodiafiltration (CVVHDF)

CVVHDF combines diffusion through dialysate with convection through ultrafiltration and therefore uses both dialysate and replacement fluid.

Qd contributes to diffusive clearance, while ultrafiltrate and the sieving coefficient contribute to convective clearance. This modality allows both mechanisms to operate in the same circuit, but it does not automatically imply higher clinical clearance or a better outcome than CVVH or CVVHD when the actual delivered dose and other conditions are equal [1–3].

In CVVHDF, the outgoing effluent volume consists of dialysate plus the total ultrafiltrate; the total ultrafiltrate includes replacement fluid and net fluid removal. Actual clearance cannot be inferred from the sum of flow rates alone without accounting for predilution, interruptions, and the properties of the solutes and the membrane.

The KDIGO recommendation for an actual or delivered effluent dose of 20–25 mL/kg/h applies to continuous therapy in general; it is not a rate specific to QUF or to CVVHDF alone [1,2].

Illustrative Example:

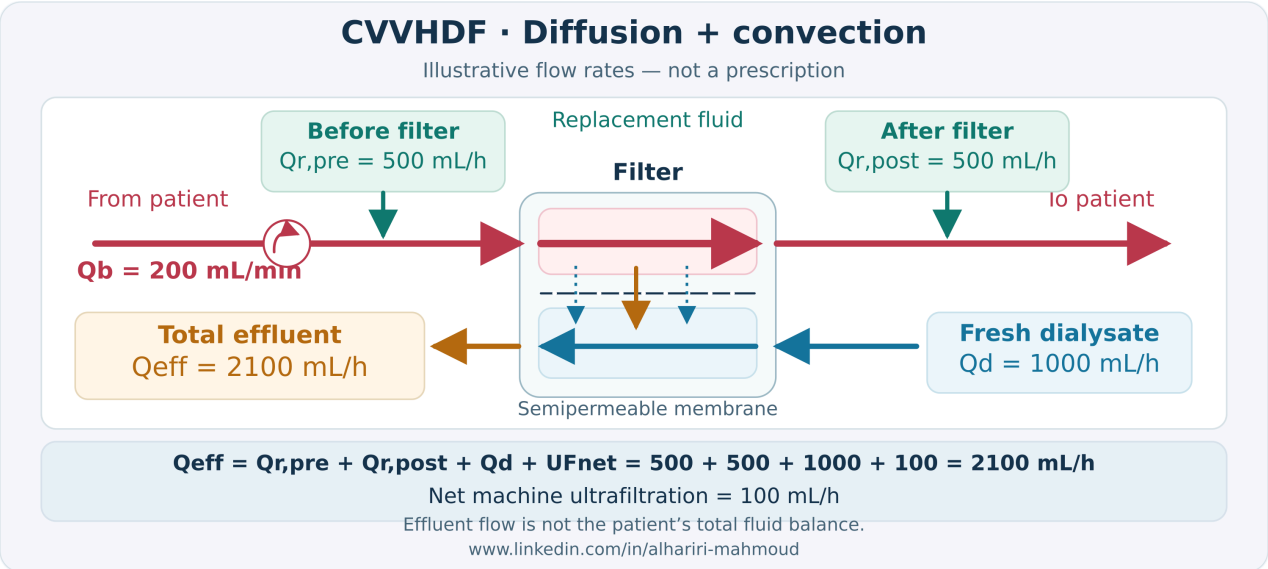
Qb 200 mL/min

Qr 500 mL/h before the filter and 500 after it.

Qd 1000 mL/h

UFnet 100 mL/h

Qef equals 2100 mL/h.



4. Slow Continuous Ultrafiltration (SCUF)

SCUF usually uses neither dialysate nor replacement fluid; its purpose is to remove fluid slowly. Ultrafiltrate is generated by the hydrostatic pressure difference across the hemofilter, and the blood flow rate Qb is usually 100–200 mL/min.

Solutes capable of crossing the membrane are transported with the water; clearance is therefore not zero, but is limited compared with modalities designed to remove solutes by diffusion or by large volumes of convection.

This modality is selected when the primary objective is fluid removal, rather than correction of a solute disturbance requiring therapeutic clearance. [1,3]

In the UNLOAD trial, venovenous ultrafiltration was compared with intravenous diuretics in patients with acute heart failure; the two primary endpoints were change in weight and dyspnea at 48 hours, and no statistically significant difference in mortality was observed. In CARRESS-HF, which included 188 patients with acute heart failure, an increase in creatinine, and persistent congestion, ultrafiltration was compared with stepped pharmacological therapy; the change in kidney function at 96 hours was more favorable with pharmacological therapy, weight loss was similar, and more serious adverse events were recorded in the ultrafiltration group. [6,7]

Components and Blood and Fluid Pathways

The circuit usually consists of a dual-lumen vascular access (dialysis catheter), a blood pump, a filter, pumps for dialysate or replacement solutions, and systems for pressure monitoring and fluid balancing.

Safe operation requires compliance with the instructions for the device and filter and with the protocol adopted by the unit.

Net Ultrafiltration and Fluid Balance

In circuit equations, UFnet denotes net ultrafiltration at the device level, i.e., the net removal of water from the circuit after accounting for replacement solution. This does not automatically equal the patient's net fluid balance; the patient's balance includes all fluid entering and leaving the body.

Pressure Monitoring in the Dialysis Circuit

The names of the pressure measurement sites and their precise definitions vary by device.

In the following schematic, the symbols denote:

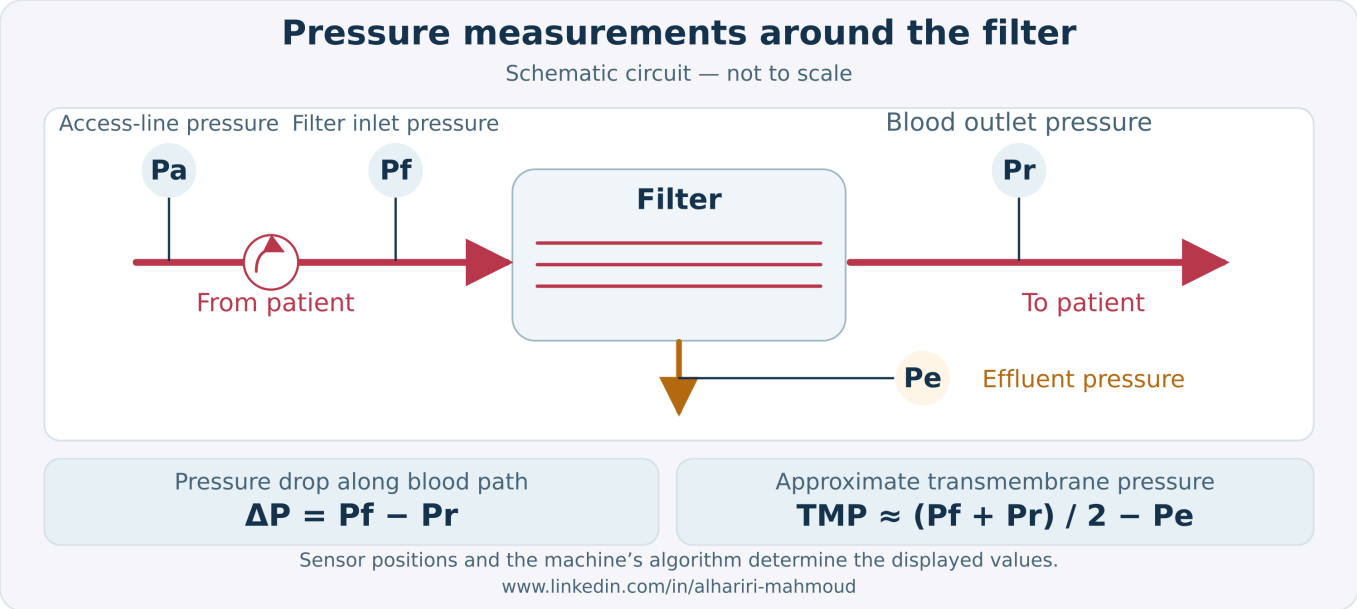
• Pa denotes the pressure in the vascular access line before the blood pump (conventionally termed the arterial or red line).

• Pf denotes the pressure between the blood pump and the hemofilter, also called filter pressure.

• Pr denotes the pressure in the line returning blood to the patient (conventionally termed the venous or blue line).

• Pe denotes the pressure in the effluent line.

Representation of the pressures ΔP and TMP



The pressure within the filter itself cannot be measured easily, but it can be estimated by taking the mean of the pressures at the filter inlet and outlet. Thus, the approximate filter pressure equals (Pf + Pr) / 2.

In general, the device manufacturer’s definitions should be used.

Pressure Interpretation

Circuit pressures are interpreted relative to baseline values after treatment starts, at a known blood flow. Withdrawal pressure before the blood pump is usually negative and becomes more negative as resistance to blood withdrawal increases. Return pressure rises when resistance in the return pathway increases. Both are affected by blood flow and by the position of the catheter, the patient, and the tubing.

The blood-side pressure drop across the filter, ΔP, is the difference between the pressures at its inlet and outlet. An increase at a constant Qb may indicate increased resistance within the filter. TMP expresses the pressure difference between the blood and fluid sides. It may rise when membrane permeability decreases or flow conditions change, but it is not a stand-alone test for diagnosing the type of obstruction.

Practical Approach to Alarms

Sign	Possible causes	Initial checks
Withdrawal pressure becoming more negative	Kinking of the withdrawal line; catheter opening abutting the vessel wall; malposition; thrombus; Qb exceeding access capacity	Inspect the line and clamps; relate the alarm to position; assess the function of both lumens and the catheter; review flow
Elevated return pressure	Kinking of the return line; obstruction or malposition of the return lumen; resistance in the return pathway	Inspect the tubing, clamps, and return pathway; assess the catheter before assuming filter clotting
Increased ΔP across the filter	Increased resistance within the fibers; possible clotting; change in blood flow	Compare values at a similar Qb; review the appearance of the circuit, anticoagulation, and filter run time

Sign	Possible causes	Initial checks
Increased TMP with a change in effluent pressure	Reduced membrane permeability, a problem in the effluent pathway, or a change in filtration settings	Inspect bags, tubing, and sensors; review QUF; interpret the trend together with ΔP and efficiency
Air or blood leak alarm	Air entry; a loose connection; a chamber or sensor fault; an actual leak across the membrane	Apply the device-specific safety procedure; check the circuit; decide on replacement and blood return according to the cause of the alarm and the protocol

This table should be viewed as a framework for investigating the cause, not as a substitute for the device instructions. Several causes may contribute to the same alarm; therefore, not every rise in TMP should be attributed to “pore clogging,” and TMP and ΔP do not both have to rise for clotting to be present.

Flow Dysfunction and Underdelivery

The device may appear to maintain a correct prescription, but recurrent alarms stop the pump and reduce treatment time. Reversing the two catheter lines may temporarily improve flow, but may increase recirculation; success therefore does not prove that the cause has been corrected. Access function should be reassessed when interruptions recur or clearance decreases despite correct settings.

Practical Points

Record the type and timing of the alarm, Qb, the patient’s position, and pressures before and after intervention. Inspect the access, tubing, and effluent pathway before increasing anticoagulation. When an overt clot, blood leak, or circuit contamination is suspected, follow the device-specific safety protocol when deciding whether to continue or replace the circuit and return the blood.

Vascular Access Dysfunction

Vascular access dysfunction often manifests as extreme, abnormal values of each of the following:

Pa, which becomes very negative.

Pr, which becomes very positive.

Hemofilter Pore Clogging

With clogging, the blood pathway through the filter remains open, but the membrane pores become obstructed as a result of protein adherence (adsorption). This causes an increase in transmembrane pressure, TMP, without a substantial change in the pressure drop across the filter, Δ(P).

Adsorption is the binding of certain substances to the membrane surface or structure. Its capacity and selectivity vary with the material used to manufacture the membrane, and its effectiveness may diminish with saturation.

Filter Clotting

Clotting commonly raises the blood-side pressure drop and may also raise TMP as usable membrane area decreases. These changes need not occur together. Interpret pressure trends with the flow settings, line pressures and device instructions.

Modern Filter Characteristics

Modern CKRT devices use hollow-fiber high-flux hemofilters, which can be used for hemodialysis or hemofiltration. High-flux filters have become the usual standard in developed countries for both IHD and CKRT.

The term high-flux refers to the membrane’s ability to remove larger substances during hemodialysis; internal filtration and backfiltration contribute particularly to the removal of larger substances.

High-flux membranes remove some middle molecules, but no single molecular-weight cutoff applies to every high-flux dialyzer. The illustrative figures of approximately 10,000 daltons for high-flux filters and 1000 daltons for historical low-flux IHD filters are schematic comparisons, not universal performance limits. Molecular-size performance must be specified for the particular membrane and test conditions.

Likewise, an illustrative value of approximately 40,000 daltons for hemofiltration is not a universal cutoff; it requires a specified filter and test conditions. Membrane permeability must be distinguished from achieved in-vivo clearance. Nominal size limits may overestimate actual performance, because plasma protein adsorption can reduce effective membrane-pore size within hours of use.

The Difference between Flux and Efficiency

In contrast to flux, efficiency describes the maximum small-molecule clearance that a particular filter can intrinsically achieve. This efficiency primarily reflects:

- Membrane surface area.

- Membrane permeability to solutes.

Because clearance during continuous dialysis is usually limited by Qd and/or Qr, the filters used in these devices are generally less efficient than those used in intermittent hemodialysis (IHD), owing to their smaller surface area. For example, approximately 1 m^2 in CKRT and approximately 2 m^2 in IHD are typical adult sizes.

Membrane Charge and Adsorption

Membrane charge influences solute removal to some extent (particularly the removal of middle molecules by convection), and also affects the tendency of solutes to adsorb onto the membrane.

In general, medium-sized and large molecules are less likely to adsorb onto uncharged membranes, such as those made of polyarylethersulfone (PAES), than onto negatively charged membranes, such as AN69 membranes composed of a copolymer of acrylonitrile and sodium methallyl sulfonate.

Membrane charge alone is insufficient to predict pore clogging; membrane composition, blood interactions and operating conditions also matter.

Removal of Larger Molecules during Hemodialysis

Although small solutes are removed during hemodialysis mainly by diffusion, larger solutes are removed predominantly as a result of the internal filtration and backfiltration that occur during hemodialysis.

What Is Meant by Internal Filtration and Backfiltration?

This is the movement of water across the dialyzer membrane in two different directions during the same high-flux HD session, because the transmembrane pressure difference changes along the capillaries. This phenomenon is well recognized in high-flux membranes.

Explanation:

In the portion near the blood inlet, the hydrostatic pressure within the blood capillaries is relatively high, so the local TMP is directed from

Blood → membrane → dialysate

An amount of plasma water therefore crosses into the dialysate compartment; this is internal filtration or direct filtration. As the water crosses, it carries with it substances capable of passing through the membrane: convection / solvent drag occurs. This is therefore particularly important for removing middle molecules that diffuse slowly, such as β_2-microglobulin.

As the blood advances toward the end of the filter, the blood pressure within the capillaries decreases because of resistance along the fibers, while the dialysate pressure also changes. The sign of TMP may therefore reverse at this point, becoming:

Dialysate → membrane → blood

An amount of dialysate water then enters the blood through the membrane; this is called backfiltration.

A very important point is that backfiltration by itself does not remove toxins from the blood, but the combination of internal filtration + backfiltration permits a large volume of internal convective fluid movement, even when the net ultrafiltration required from the patient is small.

The high permeability of a high-flux membrane allows internal filtration and backfiltration along the filter, generating internal convective transport that enhances the removal of medium-sized and relatively large molecules compared with diffusion alone.

In online HDF, this principle is amplified greatly and in a controlled manner: a large volume of plasma water is removed by convection and then replaced with substitution fluid. Middle-molecule removal is therefore usually much greater than with conventional high-flux HD. This distinction is confirmed by the latest consensus document from

EuDial/ERA. The important safety point is that, because backfiltration means dialysate can pass toward the patient's blood, dialysate purity, particularly ultrapure dialysis fluid, is critically important to avoid the transfer of contaminants and endotoxin fragments.

Solute Clearance

Once adsorption is no longer a major route of removal, effluent measurements can estimate clearance. For a solute absent from incoming treatment fluids, measured effluent-based systemic clearance is Clearance = Qef × Cef / Cp, using an undiluted systemic plasma concentration Cp. If the plasma sample is taken after predilution, adjust the reference concentration appropriately; do not apply a second dilution correction when Cp is already systemic. For a solute present in incoming fluids, including potassium when present in the solution, account for that input in the net mass balance. For pure ultrafiltrate, the sieving coefficient is:

$S = Cuf / Cp,filter$

where:

Cef is the solute concentration in the effluent; Cuf is its concentration in pure ultrafiltrate. The ratio for dialysate or mixed effluent is a saturation ratio, not automatically the sieving coefficient.

Cp,filter is the corresponding local plasma concentration used to define sieving, accounting for any predilution. It is distinct from the undiluted systemic Cp used above. The membrane reflection coefficient (σ) is related to the sieving coefficient in the following simplified model:

$S = 1 - \sigma$

The relationship $S = 1 - \sigma$ depends on the definition of the coefficient and the model; it is not an absolute equality under all transport conditions.

A solute with a sieving value of S = 1 passes freely through the filter, whereas a substance with S = 0 does not cross the membrane at all. For middle molecules, clearance depends on membrane characteristics and the ultrafiltration volume, i.e., convective clearance. For substances that undergo adsorption, removal from the blood may exceed the calculated transfilter clearance even when S is low, resulting in a discrepancy between clearance from the blood and clearance across the filter.

Removal of Inflammatory Mediators

It is worth noting that the middle molecules that can be removed or adsorbed during hemofiltration include several inflammatory mediators, such as IL-1, IL-6, IL-8, and tumor necrosis factor-α. Convective removal of these cytokines using high-volume hemofiltration (HVHF) has been studied as a treatment in patients with septic acute kidney injury, septic shock, after cardiac surgery, and in other critical conditions.

Although some studies have shown that HVHF may reduce the need for vasopressors, randomized controlled trials have not demonstrated a benefit in important clinical outcomes, such as mortality or recovery of kidney function. Trials have also not demonstrated definite superiority of CVVH, CVVHD, CVVHDF, or any particular device.

Consequently, in many centers, the choice of CKRT modality or device ultimately depends more on local device availability and local practice patterns than on theoretical differences between solute removal mechanisms or on the specific characteristics of each device.

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Vascular Access and Catheters

Catheter and Site Selection

CKRT requires a dual-lumen central venous catheter, e.g., a Shaldon catheter, that efficiently provides the required blood flow.

The KDIGO guidelines suggest initiating treatment in AKI with a nontunneled, noncuffed catheter, with the following site order: right internal jugular, then femoral, then left internal jugular, reserving the subclavian vein as the last option to reduce the risk of central venous stenosis in patients with AKI. [1]

Suggested Site Order

1. Right internal jugular vein (right IJV).
2. Femoral vein, v. fem.
3. Left internal jugular vein (left IJV).
4. Subclavian vein; last option, V. sub cl.

Insertion and Care

The KDIGO guidelines recommend using ultrasound when inserting a catheter into the internal jugular or femoral vein. Infection-control precautions and catheter care are applied according to the institution’s protocol and the adopted guidelines. Catheter size and length are selected according to the insertion site, CKRT prescription, and device, and the function of each lumen is checked before treatment starts.

Jugular versus Femoral Venous Access

In the randomized CATHEDIA trial involving 750 patients, the overall catheter colonization rate did not differ significantly between the two sites, and catheter-related bloodstream infection rates were similar. A difference according to body mass index emerged in a subgroup

analysis: catheter colonization was lower at the femoral site in patients with BMI below 24.2, and lower at the jugular site in those with BMI above 28.4. These are findings from a trial and a subgroup analysis; site selection is also balanced against patient factors and the team’s experience. [2]

Fistula and Vascular Graft (Fistula or Shunt)

Using an arteriovenous fistula or vascular graft for CKRT access requires special precautions to protect the vascular access and reduce the risks of bleeding, thrombosis, or shunt injury. The decision to use it is based on the condition of the access and the team’s assessment; it is not treated as a routine alternative to a central catheter. [1]

Catheter Care

The need for the catheter is reviewed daily, and it is removed when no longer needed. Reducing infection risk includes disinfecting the skin and connections, caring for the dressing, and minimizing unnecessary opening of the circuit. Dialysis-catheter-specific prevention instructions are followed; recommendations for other central catheters should not be generalized to ointments at the dialysis catheter exit site without considering exceptions and the preparation’s compatibility with the catheter material.

The locking solution, its concentration, and its volume are selected according to the catheter and the adopted protocol. The lock volume is related to the internal volume of each lumen, and administering an excessive volume may allow the solution to enter the circulation. Citrate used for catheter locking must also be distinguished from citrate used for regional anticoagulation during CKRT; evidence for one does not establish the effectiveness of the other.

It should not be concluded that citrate is superior to heparin for all catheter-locking outcomes, at all concentrations, and in all catheters. Antimicrobial locking solutions are likewise reserved for specific indications according to institutional policy, because their benefits and risks depend on their composition and the context of use.

Catheter-Locking Solution and Replacement

The catheter-locking solution is determined according to the catheter type, the approved lock concentration, and institutional instructions. A trial of anticoagulation within the circuit does not establish that the catheter-locking solution is the same or has the same clinical effect. [1] Heparin or trisodium citrate can be used as catheter-locking solutions after insertion and before starting CKRT, or during treatment interruptions.

A general superiority of trisodium citrate over heparin as a lock for nontunneled dialysis catheters in the intensive care unit has not been established. VERROU-REA found no significant differences between citrate 4% and heparin in event-free catheter survival, thrombosis, catheter-related infections, or adverse events. This does not establish universal equivalence or apply to every catheter setting. (Quenot JP, et al. Ann Intensive Care. 2019;9:75. doi:10.1186/s13613-019-0553-4.) For infection prevention:

• Antimicrobial-impregnated catheters are not a universal routine requirement. CDC lists them as an additional option when infection rates remain high despite comprehensive prevention and catheter duration is expected to exceed five days. [3]

• For nontunneled dialysis catheters in critically ill patients with AKI, KDIGO suggests not using topical antibiotics at the insertion site (2C). In contrast, CDC recommends suitable antiseptic or antibiotic ointments for hemodialysis catheter exit sites, subject to compatibility with catheter material. The clinical setting matters. [1,3]

• Antibiotic locks are not routinely recommended for nontunneled AKI dialysis catheters. For long-term catheters with recurrent bloodstream infections despite optimal asepsis, CDC guidance may support antimicrobial lock prophylaxis. Potential disadvantages include: [1,3]

• The occurrence of fungal infections.

• And the development of antimicrobial resistance.

Catheters are not routinely replaced solely to prevent infection; institutional guidelines are followed when infection, obstruction, or dysfunction is suspected. [3] When it becomes clear that recovery of kidney function sufficient to discontinue KRT is not imminent, placement of a permanent dialysis catheter, such as a tunneled cuffed hemodialysis catheter or a Demers catheter, should be considered.

Exchange of a malfunctioning temporary dialysis catheter over a guidewire may fail to resolve dysfunction. A new insertion site may be appropriate in selected cases, depending on the cause, access options and infection risks. [4]

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Anticoagulation

Choosing an Anticoagulation Strategy

Although the 2012 KDIGO guidelines for acute kidney injury (AKI) recommend anticoagulation to prolong filter life, a substantial proportion of centers, estimated at approximately 33%–50%, initiate CKRT without anticoagulation and subsequently add anticoagulation if early filter clotting occurs. Heparin and citrate are the most commonly used anticoagulants in CKRT.

KDIGO suggests regional citrate rather than heparin for anticoagulation during CKRT in appropriate patients without contraindications to citrate (conditional recommendation, grade 2B). The necessary expertise, a defined protocol and a specified monitoring regimen are required [1].

Heparin

Heparin has the advantages of low cost and familiar clinical use, and it can be administered either through a separate intravenous pump or into the CKRT circuit upstream of the filter. Administration into the circuit before the filter is preferred because it increases the heparin concentration within the filter. However, heparin cannot be removed by dialysis, so prefilter administration still produces systemic anticoagulation unless a reversal agent, or antidote, is used with it. Less commonly, heparin is used with the reversal agent protamine to achieve anticoagulation confined to the dialysis circuit. As expected, heparin use without reversal of its effect is associated with an increased risk of bleeding.

When HIT is suspected, its clinical probability is assessed and sources of heparin, including catheter lock solutions, are discontinued when indicated. If HIT is acute and requires systemic anticoagulation, RCA alone does not address the systemic thrombotic risk; a non-heparin anticoagulant is selected according to the clinical situation and organ function. This point is based on the ASH guidelines and is not a finding from a trial comparing CKRT modalities. [4]

Regional Citrate Anticoagulation (RCA)

Unlike heparin, RCA does not produce systemic anticoagulation. In this method, citrate is administered into the circuit upstream of the filter, usually with the aim of achieving a circuit citrate concentration of 3–6 mmol/L. Citrate doses, infusion sites, and laboratory targets differ according to the solution, device, and protocol; numerical targets must therefore not be transferred between protocols without verification [1, 3].

Citrate chelates calcium (binding and inactivating it), reducing the ionized calcium concentration within the filter to a low level, usually below 0.4 mmol/L, thereby inhibiting the coagulation cascade within the filter.

Calcium is usually replaced in the patient through a separate infusion (or, more commonly, immediately before the filtered blood is returned to the patient) to maintain the systemic ionized calcium level. The RICH trial compared regional citrate with systemic heparin in critically ill patients. Median filter life was 46.5 hours with citrate and 26 hours with heparin. Bleeding complications were less frequent in the citrate group, at 5.1% versus 16.9%, whereas new infections were more frequent, at 68.0% versus 55.4%. The trial did not demonstrate a significant difference in 90-day mortality, and its ability to establish the effect of the strategy on mortality was limited because it was stopped early [2].

Citrate Disposition during CKRT

Most citrate is usually removed in the CKRT effluent. Nevertheless, a variable but substantial proportion reaches the patient, where it is metabolized primarily in the liver (and to a lesser extent in the muscles and kidneys). To reverse the effect of citrate, replace the calcium lost (as citrate–calcium complexes), and prevent life-threatening hypocalcemia, calcium must be administered continuously by the intravenous route. It can be given (as mentioned previously):

In the return limb of the CKRT circuit leading to the patient.

Or through a separate calcium pump.

The citrate dose is adjusted in relation to blood flow and according to postfilter ionized calcium, whereas the calcium infusion is adjusted according to systemic ionized calcium. Many

protocols target a postfilter ionized calcium level of approximately 0.25–0.35 mmol/L, but the accepted range depends on the protocol and measurement method. Infusion rates expressed in mL/hour must not be transferred between citrate preparations of different concentrations. [2, 5]

Calcium and Citrate Monitoring

Standard RCA protocols include serial monitoring of both ionized calcium within the filter and systemic ionized calcium in the patient's blood, allowing adjustment of the citrate and calcium infusion rates.

If ionized calcium within the filter is above the target, the citrate infusion rate is increased, and vice versa.

If systemic ionized calcium is low, the calcium infusion rate is increased, and vice versa.

Finally, as will be explained later, total calcium should be monitored at least once daily to detect possible citrate accumulation. Several different citrate formulations are available for anticoagulation, and each requires its own protocol for use.

RCA in Patients with Liver Disease

Historically, liver disease was considered a contraindication to RCA (because citrate is metabolized primarily in the liver). However, recent data indicate that RCA can be used in patients with liver disease with close monitoring. Notably, the coagulation disorders associated with liver disease are accompanied by both an increased risk of bleeding and an increased risk of thrombosis; liver disease is therefore also associated with shorter CKRT filter life. Specific protocols have been developed to reduce the risk of citrate accumulation when citrate is used in situations in which its metabolism is absent or severely impaired. [6]

The Delphi consensus published in 2026 indicates that it may be used cautiously in severe shock and severe liver failure when expertise and monitoring are available; these are expert consensus recommendations, not evidence from randomized trials establishing the safety of all protocols in these groups. [6]

Conventional liver tests are insufficient to assess the capacity to metabolize citrate. The lactate trend, perfusion, blood gases and electrolytes, calcium requirements, and the ratio of total to

ionized calcium are reviewed alongside them. If these parameters deteriorate, the strategy is promptly reassessed, including reducing or discontinuing the citrate load and selecting an alternative according to the cause.

Distinguishing Alkali Overload (Metabolic Alkalosis) from Citrate Accumulation

Citrate may be metabolized to bicarbonate; citrate loading may therefore be associated with increased bicarbonate and metabolic alkalosis. Citrate accumulation, by contrast, occurs when the body's capacity to metabolize citrate is reduced and may present with low ionized calcium or an increased total-to-ionized calcium ratio. These parameters are interpreted in the clinical context and in light of trends in serial results; no single parameter is relied upon. For details, see Complications [1, 3].

Monitoring and Metabolic Differentiation between Disorders

Parameter	What guides its interpretation — Clinical interpretation
Postfilter ionized calcium — Postfilter iCa	Adequacy of anticoagulation within the circuit; review the sample and target before adjusting citrate.
Systemic ionized calcium — Systemic iCa	The patient's calcium balance and the need to adjust replacement.
Total calcium and the tCa/iCa ratio	An increased ratio and its trend may support citrate accumulation; units of measurement must be consistent.
Increasing calcium requirements	May be a warning sign of citrate accumulation or increased losses; interpret together with the other results.
pH, bicarbonate, and the anion gap	Distinguishing alkalosis caused by an alkali load from acidosis and mixed disorders.
Sodium, magnesium, and lactate	The effects of solution composition, losses, and perfusion status; trends in values and the context are what matter.

Lactate as a Marker of Citrate Accumulation Risk

Lactate concentration and its trajectory may help assess the risk of citrate accumulation. In a retrospective cohort, the positive predictive value of baseline lactate was limited and lactate kinetics was more informative. (Khadzhynov D, et al. Crit Care Med. 2017;45:e941-e946. doi:10.1097/CCM.0000000000002501.) Lactate and citrate are metabolized in the liver and other metabolically active tissues.

An elevated lactate level may result from increased production, reduced elimination, or both. It therefore does not prove impaired metabolism regardless of cause, nor does it establish citrate accumulation on its own.

A universally validated risk classification based only on fixed lactate ranges has not been established. Assessment combines:

Lactate trajectory and the response to treatment of its cause.

Hemodynamics, tissue perfusion, and acid-base status.

Systemic ionized calcium, total calcium/ionized calcium in the same molar units, and increasing calcium replacement requirements. [5]

RCA versus Systemic Heparin

Citrate use for RCA increases treatment complexity and requires more frequent laboratory monitoring. Nevertheless, trials have repeatedly shown the superiority of RCA over systemic heparin with regard to:

Prolonging filter life.

Reducing bleeding complications.

The most recent and largest of these studies was the multicenter RICH trial, which randomized approximately 600 patients to: [2]

Systemic heparin.

Or regional citrate anticoagulation.

The study showed that RCA, compared with systemic heparin, resulted in:

A marked prolongation of filter life by approximately 15 hours.

Fewer bleeding events.

No significant difference in the mortality rate.

Monitoring and Safety

RCA protocols require training and continuous monitoring. These points do not constitute a treatment prescription and do not define numerical laboratory targets; the operational reference is the institution’s protocol and the device instructions [1, 3].

Monitor systemic and circuit ionized calcium at the frequency specified in the local protocol.

Monitor total calcium, electrolytes, bicarbonate, and blood gases according to the patient’s condition and the unit protocol.

Reassess calcium and citrate balance when the metabolic state or hepatic and circulatory function changes.

Escalate to the specialist team if an acid–base disorder or a worsening calcium disorder develops.

Heparin and Other Anticoagulants

Systemic heparin is used in some cases, with assessment of bleeding risk and contraindications and monitoring of coagulation according to the protocol [1]. The comparative evidence from the RICH trial concerns citrate and heparin under the conditions of that trial and cannot automatically be generalized to all anticoagulants or all patients [2].

Alternative Anticoagulants for CKRT

Less commonly used options for anticoagulation within the CKRT circuit include

Direct thrombin inhibitors.

Nafamostat mesylate, a serine protease inhibitor that has been used for decades in East Asia. However, to date, no large randomized controlled trials have adequately evaluated the use of these options. [2, 4]

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Fluid Management

Solutions and Fluid Balance during Continuous Kidney Replacement Therapy

CKRT Solutions and Their Composition:

Dialysate and replacement solutions differ primarily in their concentrations of sodium, potassium, and bicarbonate, as well as calcium, magnesium, phosphate, and glucose. This allows precise, simultaneous, and independent management of fluid balance and plasma composition.

For example, the plasma sodium concentration can be maintained at any target value while the fluid balance is kept neutral, negative, or positive. The composition should be selected according to serial laboratory results, the treatment prescription, and the local protocol, with a review of the solution's compatibility with the anticoagulant and device [1, 4].

Disorders of Blood Sodium

Using standard sodium solutions in a patient with severe hyponatremia may result in faster correction than intended.

Strategies have been described that include low-sodium solutions or the addition of 5% dextrose in water (D5W) to the circuit; the method and its rate depend on the prescription, effluent rate, target sodium concentration, and monitoring of blood sodium [1, 2].

On conventional IHD proportioning systems, dialysate sodium is adjusted through the machine prescription/conductivity control and compatible concentrates, within the manufacturer-approved range. A range such as 130–145 mmol/L is illustrative, not universal; follow the specific device instructions. Achieving effective sodium concentrations outside the approved range is difficult with conventional IHD, partly because of its relatively high Qd. In CKRT, although sodium concentrations in premade solutions are fixed, the relatively lower Qd and Qr allow the effective sodium concentration to be adjusted more easily, enabling slow, controlled correction of severe hyponatremia or hypernatremia.

Mixing equations can be used to estimate the final sodium concentration in the circuit, but the calculation alone does not constitute a clinical correction plan. Implementation requires frequent sodium monitoring, and any D5W must be counted as part of the patient's fluid intake [1, 2].

Correction of Severe Hyponatremia Using CKRT

Starting CKRT with a solution containing 140 mmol/L sodium in a patient with severe hyponatremia may lead to more rapid correction than intended. The plan is determined by symptom severity, the duration of the disorder, and the risk of osmotic demyelination syndrome (ODS). [5]

In chronic hyponatremia or hyponatremia of unknown duration, particularly when the risk of ODS is high, a conservative increase of approximately 4–6 mmol/L over 24 hours is usually targeted, and an increase exceeding 8 mmol/L in any 24-hour period is avoided in high-risk patients. These limits apply to the actual blood sodium concentration, taking account of all causes of its change.

Severe neurological symptoms require appropriate emergency treatment in parallel with CKRT. Sodium may rise because of the onset of water diuresis, potassium replacement, or a change in intake, even if the device settings do not change. The solution equation alone is therefore insufficient to predict the course of blood sodium.

The effective sodium concentration in the solution can be lowered by:

1. Diluting the CKRT solution by adding sterile water to the bag.

2. Or removing part of the CKRT solution and replacing it with sterile water. However, this method is generally impractical when commercially prepared solutions are used, because large quantities of sterile water are not routinely available in hospitals owing to the risk of its accidental systemic administration to the patient. Adding fluid to or withdrawing fluid from ready-to-use sterile bags also carries risks of inaccuracy or loss of sterility. Institutions where CKRT solutions are prepared in the pharmacy may be better able to customize low-sodium solutions, but this approach in turn carries a risk of preparation errors and microbial contamination.

Using D5W to Modify Sodium

Another approach when using commercially prepared solutions is to administer an additional infusion of Dextrose 5% in Water — D5W. It may be given into the CKRT circuit, usually after the filter, or through a separate systemic infusion.

For patients with hyponatremia, the additional D5W flow in liters per hour can be estimated with the following simplified mixing equation. The target here is the effective sodium concentration of the mixture:

$VD5W = Qef \times ([Na^+]CKRT - [Na^+]T) / [Na^+]T$

Where:

VD5W is the volume of D5W in liters/hour.

In this equation, Qef is the baseline therapy flow in liters/hour before the additional D5W is included, not the final total flow after its addition. $[Na^+]CKRT$ is the sodium concentration in the dialysate and/or replacement solution, and $[Na^+]T$ is the target mixing concentration.

Example:

For a target mixing concentration of 125 mmol/L, a CKRT solution containing 140 mmol/L sodium and a baseline therapy flow of 2.5 liters/hour before the additional D5W, the calculation is:

$VD5W = 2.5 \times (140 - 125) / 125$

$= 0.3$ L/h

That is:

The calculated additional D5W flow is 300 mL/hour. Specify the infusion site and all component flows, and account for this additional volume in the prescribed fluid balance and ultrafiltration setting.

The UFnet setting displayed on the device differs depending on whether it counts D5W among the replacement fluids or as an external intake. The value 125 here is the target mixing concentration in the model, not a prediction of the patient's blood sodium after one hour, nor a target to be selected automatically. Use of this relationship requires specification of the infusion site, the method of calculating flows, and whether D5W is included in the device's fluid balance, as well as accounting for other fluids and citrate when present. [1]

Increasing Effective Sodium Concentration

When CKRT solutions with a high effective sodium concentration are required, either to correct severe hypernatremia gradually or to achieve therapeutic hypernatremia, hypertonic saline can be used in one of two ways:

1. Adding it to CKRT solutions, usually using 23.4% sodium chloride.

2. Or infusing it into the CKRT circuit or systemically, usually using 3% sodium chloride.

Example

For a patient weighing 60 kg, 25 mL/kg/hour corresponds to 1500 mL/hour. This mixing example assumes CVVH with 1.5 liters/hour of postfilter replacement: 140 mmol/L × 1.5 liters/hour = 210 mmol/hour of sodium in the incoming solution. This is not net sodium balance, because sodium is simultaneously removed in ultrafiltrate. In CVVHD, dialysate is not infused into the patient. [1,2]

A 3% sodium chloride solution can then be infused at 50 mL/hour, either into the CKRT circuit, usually as a postfilter replacement solution, or through a separate intravenous line. A 3% sodium chloride solution contains 513 mmol/L.

The additional sodium delivered at an infusion rate of 50 mL/hour is therefore: 513 mmol/L multiplied by 0.05 liters/hour (50 mL/hour), giving 25.7 mmol/hour of additional sodium.

Combining the two sources:

210 mmol/hour from the replacement solution + 25.7 mmol/hour from the additional infusion gives 235.7 mmol/hour in 1.55 liters/hour of incoming solution. This is not the amount of sodium retained in the body. The additional fluid must be included in fluid balance and the UFnet prescription.

The calculated sodium concentration of this mixture is:

235.7 mmol/hour ÷ 1.55 liters/hour = 152 mmol/L

The clinical aim is to reduce the gradient between the initial serum sodium of 154 mmol/L and CKRT solution containing Na 140 mmol/L. Under these assumptions, the additional 3% NaCl infusion gives approximately 152 mmol/L. In cerebral edema and intracranial hypertension, the sodium target and trajectory require close monitoring; the mixture value does not guarantee stable hypernatremia. CVVHD and CVVHDF require modality-specific sodium balance using actual clearance. [1,2]

Summary: Na 140 mmol/L describes the base solution, 152 mmol/L the calculated mixture with 3% NaCl, and 154 mmol/L the initial serum value. The serum value after one hour requires a kinetic model accounting for total body water, all sodium and water inputs and outputs, residual kidney function, and interruptions; it does not immediately become 152 mmol/L. Serial monitoring is required. [1,2]

Potassium and Bicarbonate in CKRT Solutions

Continuous therapy may permit potassium control with a higher potassium concentration in the therapy fluid than some intermittent prescriptions. Daily clearance depends on the prescription and treatment actually delivered, including interruptions; the qualifications accompanying the comparison table also apply here. A potassium concentration of 4 mmol/L is often sufficient unless hyperkalemia is severe, but the solution must be selected using serial potassium measurements and the clinical context. Acetate or lactate were historically used as the principal buffers in KRT solutions, but modern CKRT solutions now rely almost exclusively on bicarbonate. The typical bicarbonate concentration ranges from 22–35 mEq/L.

CKRT Solutions with Citrate Anticoagulation (RCA)

CKRT solutions used with regional citrate anticoagulation (RCA) are usually calcium-free, which facilitates lowering the calcium concentration within the filter.

These solutions also usually contain a lower bicarbonate concentration, approximately 25 mEq/L, compared with other standard CKRT solutions, which typically contain approximately 35 mEq/L bicarbonate. This is intended to account for the alkali load produced by citrate after it is metabolized in the liver. Unlike lactate, which yields an equimolar amount of bicarbonate when metabolized, each citrate molecule is metabolized to 3 bicarbonate molecules. It is also important that some commercial phosphate-containing CKRT solutions are now available, whereas conventional CKRT solutions are phosphate-free.

Achieving Fluid Balance

As mentioned previously, one of the most important practical advantages of CKRT is its ability to remove fluid continuously and gradually. CKRT devices use gravimetric or volumetric measurement techniques to measure fluid flow rates precisely. This provides much greater accuracy in volume control than conventional pumps used to administer intravenous fluids.

Distinguishing Machine UFnet from Patient Fluid Balance

At the machine level, UFnet is the device's net removal after subtracting the replacement solution rate from the total ultrafiltration rate. The patient's fluid balance, however, includes all fluid inputs and outputs, including medications, nutrition, intravenous fluids, urine, and other outputs. The UFnet value therefore does not equal the patient's overall balance [4].

Machine UFnet ≠ Patient net fluid balance

Net Ultrafiltration Prescription

There are several ways to prescribe net ultrafiltration. The most common approach is for nursing staff to make hourly adjustments to the machine's net ultrafiltration rate to achieve the prescribed targets for the patient's net fluid balance, whether these targets are hourly or daily.

Despite numerous ongoing trials, rigorous data defining the best strategy for volume management using CKRT remain insufficient. In any critically ill patient requiring CKRT, the nephrology and critical care teams should use all available data on hemodynamic and fluid status. These data should preferably include dynamic measures of volume status to guide the net ultrafiltration prescription. In addition, the constantly changing nature of critical illness requires frequent, serial reassessment of ultrafiltration targets and the patient's tolerance. [6]

Phosphate in CKRT Solutions

Many solutions used in CKRT do not contain phosphate; hypophosphatemia may therefore develop during continuous treatment. In a large observational study, phosphate-containing solutions were associated with a lower incidence of hypophosphatemia than phosphate-free solutions (21% versus 62%). This is an observational association, not proof of improved clinical outcomes [3]. Phosphate concentrations are reviewed periodically, and supplementation or a phosphate-containing solution is selected according to the laboratory result, the available formulation, and the protocol.

Monitoring Plan

1. Review blood sodium and the frequency of measurement when changing the solution’s sodium concentration or adding D5W.

2. Monitor potassium, phosphate, magnesium, calcium, and bicarbonate according to the patient’s condition.

3. Record prescribed and achieved UFnet alongside the patient’s overall fluid balance.

4. Recheck the pump setting against the treatment prescription after every change in solutions or flow rates.

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Initiation and Discontinuation of CKRT

Timing of Initiation

Treatment is initiated as an emergency when there is a life-threatening disturbance of fluid, electrolyte, or acid–base balance that cannot be controlled with appropriate treatment. Examples include refractory hyperkalemia, uncontrolled severe acidosis, pulmonary edema associated with volume overload, and uremic complications. The clinical context and trends in findings are considered, rather than an isolated creatinine or urea value.

In the absence of an emergency indication, the decision balances the patient's need for fluid and solute removal against residual kidney capacity and the anticipated course. Conservative monitoring requires reliable follow-up and readiness to initiate treatment if the condition deteriorates. Oliguria for a specified duration alone does not become an automatic indication independent of the other findings [1].

Starting CKRT later than necessary may lead to complications arising from acute kidney injury (AKI) and volume overload. Conversely, starting too early may expose patients who might not actually have needed dialysis to its potential risks.

In the STARRT-AKI trial, the accelerated initiation strategy did not reduce mortality at 90 days compared with the standard strategy, while dialysis dependence increased among survivors. This finding supports avoiding routine accelerated initiation in the absence of an urgent indication; however, it does not justify delaying treatment when a clear indication exists [2].

In AKIKI and IDEAL-ICU, no consistent benefit of early initiation was demonstrated in the patients included in the two trials. Indeed, some signals of potential harm with accelerated initiation were observed, including:

Reduced recovery of kidney function.

An increased incidence of catheter-related bloodstream infections.

Higher rates of hypotension.

And an increased incidence of hypophosphatemia. [3,4]

The more recent AKIKI-2 trial randomized patients with severe acute kidney injury who met specified inclusion criteria to a standard initiation strategy or a “more delayed” strategy. The primary outcome, dialysis-free days over 28 days, did not improve with further delay. Crude mortality at day 60 was approximately 55% versus 44%, a difference that did not reach significance in the unadjusted comparison. However, multivariable analysis showed an increased risk of death with the more delayed strategy: HR 1.65, 95% confidence interval 1.09 to 2.50, and P = 0.018.

Thus, there is no clear benefit from accelerated initiation of dialysis treatment; conversely, the study suggests that patients may be harmed if treatment is delayed excessively beyond standard initiation strategies.

Finally, it should be emphasized that trial criteria differ and should not be used as a substitute for assessing the patient [3–5].

Indications and Reassessment of Goals

For most patients, as mentioned previously, CKRT should be initiated in response to clear, tangible clinical indications, most commonly:

Volume overload that cannot be adequately managed by other means.

Hyperkalemia or a severe acid–base disorder that does not respond to appropriate management.

Uremic complications or other indications identified by the team according to the patient’s condition.

For patients considered appropriate candidates for escalation of care, initiating CKRT is also likely to be a reasonable option when oliguria persists for 48–72 hours. It is worth noting that overall mortality in these randomized trials, as well as in many other studies involving critically ill patients with AKI who require dialysis treatment, is approximately 50%.

In the absence of an indication for dialysis treatment involving an imminent threat to life, discussion of CKRT initiation should generally prompt both intensivists and nephrologists to reassess the patient’s overall prognosis. For many patients, it may be appropriate to have

a discussion with them or their representatives about goals of care before obtaining consent to initiate CKRT.

Assessment of Kidney Recovery

Whether the kidneys can meet the patient's needs without support is reassessed daily. This assessment includes improvement in the precipitating cause, circulatory stability, a reduced need for fluid removal, and trends in urine output, creatinine, and electrolytes. Increased urine output may be an early sign, but on its own it does not establish adequate solute clearance, particularly when diuretics are used.

Observational studies and reviews have proposed approximate urine-output thresholds, such as more than 500 mL/day without diuretics or more than 2000 mL/day with diuretics, for beginning to consider a trial off treatment. These are prompts for reassessment, not sufficient conditions or validated thresholds applicable to everyone. They are interpreted in relation to fluid intake and the ability to control volume.

Creatinine clearance measured from a timed urine collection may be useful if the collection is reliable and a suitably timed blood sample is obtained. However, rapid changes in plasma creatinine, the effect of ongoing CKRT, and tubular creatinine secretion all limit accuracy. The usual eGFR equations are not used as an accurate estimate of kidney function in a non-steady state. [9]

De-escalation, Discontinuation, and Transition to Another Modality

Although randomized controlled trials are ongoing, there are currently no clinical trial data (with the exception of LIBERATE-D) on which to base guidance for reducing the intensity of CKRT or discontinuing it. Decisions to discontinue CKRT or transition to intermittent treatment are generally based on recovery of kidney function, urine output, hemodynamic stability, and the patient's ability to tolerate the alternative treatment modality; these indicators are used within the clinical assessment [1].

LIBERATE D

LIBERATE-D studied patients with AKI who required dialysis but had become hemodynamically stable, with plans to continue intermittent dialysis. The study compared dialysis performed when specified metabolic or clinical indications were met with dialysis performed three times weekly until recovery criteria were met.

Recovery at discharge, as defined in the study, was 64% versus 50%, with an absolute difference of 13.8 percentage points in the unadjusted analysis. After the prespecified adjustment, however, the odds ratio was 1.56 with a 95% confidence interval of 0.86 to 2.84, meaning that the adjusted estimate did not establish the presence of a benefit. The study supports reassessing the need for each session during recovery, but it does not establish a direct criterion for discontinuing CKRT in an unstable patient, and its findings require broader confirmation. [10]

An ongoing need for vasopressors and a more positive cumulative fluid balance are also associated with hypotension during the dialysis session in patients transitioning from CKRT to intermittent hemodialysis (IHD). In general, achieving hemodynamic stability without vasopressor support is one of the common criteria prompting consideration of transition from CKRT to IHD. Experts also suggest that volume overload should be corrected before discontinuing CKRT or transitioning to another kidney replacement therapy modality.

CKRT Dose

KDIGO recommends prescribing a dose that enables an actually delivered effluent-volume dose of 20 to 25 mL/kg/h in adults with AKI receiving CKRT. [1]

Unlike intermittent hemodialysis (IHD), where pre- and post-treatment urea measurements are used to assess dose, CKRT commonly uses total effluent flow (Qef) as an approximate surrogate for freely permeable small-solute clearance. In the absence of additional circuit fluids, Qef = Qd + Qrep + Qnet. Actual clearance also depends on effluent saturation, predilution and interruptions. (Neri M, et al. Crit Care. 2016;20:318. doi:10.1186/s13054-016-1489-9.)

Used dialysate flow Qd, associated with diffusive transport.

The portion of total ultrafiltration replaced by replacement fluid Qrep.

Net ultrafiltration from the patient Qnet, which contributes to convection and is not a third independent clearance mechanism.

Although some early trials suggested a potential benefit from higher doses, two subsequent large randomized trials, the VA/NIH ATN trial and RENAL [6, 7]

showed that higher CKRT doses of 35–40 mL/kg/h provided no benefit compared with lower doses of 20–25 mL/kg/h. Instead, higher doses were associated with slightly higher rates of some complications, including:

Hypophosphatemia.

Hypotension.

Based on these two trials, the standard of care has become targeting an actually delivered CKRT dose (Delivered dose) of 20–25 mL/kg/h.

At usual settings, instantaneous small-solute clearance during CKRT is lower than during an IHD session, but the longer treatment duration may compensate. This does not establish a universally higher daily or weekly dose than three-times-weekly or daily IHD. Modality, treatment duration and frequency, interruptions, blood, dialysate and effluent flows, and the solute all matter. Comparisons require a common kinetic dose measure; a session Kt/V must not be compared directly with a CKRT effluent dose. [1] (Neri M, et al. Crit Care. 2016;20:318. doi:10.1186/s13054-016-1489-9.)

Modality	Maximal theoretical clearance (mL/min)	Approximate weekly dose Typical weekly standardized Kt/Vurea
IHD, three times weekly	280	2
IHD, seven times weekly	280	5
PD, seven times weekly	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

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Illustrative values under different model assumptions. For CKRT/IHD: body weight 60 kg, total body water 36 L, hematocrit 30%, blood flow 200/400 mL/min respectively, sieving coefficient 1 and complete dialysate saturation. CKRT estimates assume no downtime, loss of efficiency or fluid overload. IHD weekly standardized Kt/V uses a typical session spKt/V of 1.3. PD maximal clearance assumes hourly 2 L exchanges and D/Pcreatinine of 0.5; its weekly Kt/V assumes a 70 kg CAPD patient, a drain volume of 10.2 L/day and complete equilibration. These columns therefore do not use identical assumptions. [1]

The delivered dose may be lower than the prescribed dose when treatment is interrupted, because of filter clotting, or because of procedures outside the unit. The record of actual treatment hours and the achieved effluent flow rate are therefore reviewed. When calculating Qef, care is taken to ensure that the prescription components and UFnet are defined in the same way on the machine [1].

Item	Meaning
Prescribed dose	The effluent flow rate specified by the team
Delivered dose	What the patient actually received after accounting for operating time and interruptions
Measurement of treatment intensity	Effluent volume in mL/kg/h; it does not describe the clinical condition on its own

The Difference between the Prescribed and Actually Delivered Dose

In practice, several factors cause the actual achieved or delivered CKRT dose to be lower than the prescribed dose. These include:

Loss of part of the effective surface area due to filter clotting or pore blockage.

The time required to change the filter.

The need for imaging examinations or procedures outside the intensive care unit.

And other factors.

Observational studies suggest that the actually delivered CKRT dose, rather than the prescribed dose, is associated with clinical outcomes, although this relationship may be affected by confounding factors.

Empirical increases of 20%–25% have been proposed to compensate for the difference between prescribed and delivered dose. KDIGO notes that prescriptions of 25–30 mL/kg/h are often needed to deliver 20–25 mL/kg/h. Actual treatment delivery, interruptions, and predilution guide adjustment, rather than a fixed percentage. [1]

In the lower-intensity groups, ATN has been described as achieving approximately 17.5 mL/kg/h after predilution correction with a prescription of 20 mL/kg/h, whereas RENAL delivered approximately 22 with a prescription of 25 mL/kg/h. (Prowle JR, Schneider A, Bellomo R. Crit Care. 2011;15:207. doi:10.1186/cc9415.) Each trial found no benefit from greater intensity within its randomized comparison. Different dose definitions do not establish direct equivalence across 17.5–22 mL/kg/h or a universal prescription ceiling of 25 mL/kg/h. [6,7]

Can Doses below 20 mL/kg/h Be Used?

Although this remains controversial, it is theoretically possible that prescribed doses below 20 mL/kg/h are no less effective than standard doses. Trials investigating this are ongoing, but there are currently no randomized controlled trial data supporting this strategy. More comprehensive measures of the adequacy of solute removal may also be as important as the prescribed Qef, including:

Electrolyte homeostasis.

Acid–base balance

Potassium concentration

pH

Potential risks of higher delivered CKRT doses include excessive or unwanted removal of:

Electrolytes, particularly phosphate

Micronutrients

Drugs

Effect of the Replacement Fluid Administration Site on Dose

The site at which replacement fluid is administered in the CKRT circuit affects the dose, particularly in CVVH and CVVHDF.

Postfilter Replacement (Postdilution)

When replacement fluid is administered after the filter, that is, by postfilter dilution (Postdilution), convective solute removal avoids predilution-related loss of efficiency. For a freely filterable solute with a sieving coefficient (SC) of approximately 1, its concentration in ultrafiltrate approximates its local concentration in plasma water. The trade-off, however, is that filtering undiluted plasma water causes a marked increase in the concentration of red blood cells and proteins along the filter, increasing the risk of filter clotting.

Filtration Fraction

Hemoconcentration risk is often assessed using filtration fraction (FF): the total ultrafiltration rate divided by the plasma flow entering the filter. Approximately, Qplasma = Qb × (1 − Hct), where Hct is a fraction; plasma flow is used as an approximation of plasma water flow.

FF differs from concentration ratio (CR): CR = QUF/(Qb + Qr,pre). The technical consensus suggests ideally FF below 30% and CR below 20%–25%; local protocols may use stricter limits. (Neri M, et al. Crit Care. 2016;20:318. doi:10.1186/s13054-016-1489-9.) Measures to limit hemoconcentration include:

An adequate blood flow rate, Qb, for the selected measure. Without predilution, Qb = 4 × QUF gives CR = 25%, but with Hct = 0.30 it gives FF of approximately 35.7%, not 25%.

Or relatively favoring the use of prefilter replacement fluid.

Citrate anticoagulation (RCA) may be a potential exception, as clinical experience suggests that it may allow higher FF values to be used.

Clarification:

In postfilter CVVH, QUF is divided by Qplasma. With predilution, its flow is added to the denominator. All flows must use the same time unit:

FF ≈ QUF / (Qplasma + Qr,pre)

QUF = Qr,pre + Qr,post + UFnet

Some protocols use stricter FF targets below 20%–25%, especially with postdilution. The relationship between FF and clotting also depends on anticoagulation, membrane, and flows. FF reflects hemoconcentration differently during predilution; postfilter hematocrit is a proposed additional marker, but its superiority is not established.

An FF of 25% means that one quarter of the flow used in the denominator of its definition is filtered; it does not mean that one quarter of the total blood flow is filtered. The equation should therefore not be replaced by a general rule such as “Qb is four times the filtration rate” without accounting for hematocrit, the replacement site, and flow units. [12, 13]

Complete Worked Example:

For a patient weighing 70 kg, CVVH was prescribed with the following flows: Qb of 200 mL/min, prefilter replacement of 1500 mL/h, postfilter replacement of 500 mL/h, and UFnet of 100 mL/h. For this teaching example, we add a hematocrit of 0.30 and assume that there are no other infusions requiring separate accounting, and that the sieving coefficient for the solute under consideration is approximately one.

Calculation step	Calculation	Result
Effluent flow Qeff	1500 + 500 + 100	2100 mL/h
Nominal dose	2100 ÷ 70	30 mL/kg/h
Approximate plasma flow Qplasma	200 × 60 × 0.70	8400 mL/h
Dilution factor	8400 ÷ (8400 + 1500)	Approximately 0.848
Approximate corrected clearance Correction estimate	2100 × 0.848	Approximately 1782 mL/h
Corrected dose during operation Dose during operation	1782 ÷ 70	Approximately 25.5 mL/kg/h
Filtration fraction FF	2100 ÷ (8400 + 1500)	Approximately 21.2%

These results are calculated from the stated data using the simplified dilution model; they are not study results or a laboratory measurement of the patient’s clearance. They illustrate why the nominal value of 30 differs from the corrected clearance estimate. If the solute’s characteristics do not meet the model’s assumptions, the correction is reviewed or clearance is measured using suitable samples.

If the circuit in the preceding example operates for only 22 hours during the day and all other settings remain constant, the nominal dose achieved from the effluent volume over the entire day is:

Effluent dose over 24 h = (2100 × 22) / (70 × 24) = 27.5 mL/kg/h

The average clearance corrected for dilution according to the example’s model is:

Corrected average dose ≈ 25.45 × (22 / 24) = 23.3 mL/kg/h

The difference between the two values results from the dilution correction, whereas the reduction from the operating dose results from two hours of downtime. If the settings change during the day, the effluent volume or estimated clearance is calculated separately for each period and the periods are then summed; the end-of-day setting is not multiplied by 24 hours.

Prefilter Replacement (Predilution)

Moving part of replacement fluid before the filter (predilution) at a constant total ultrafiltration rate reduces hemoconcentration and may prolong filter life. If extra predilution fluid is added with a corresponding increase in ultrafiltration, FF must be recalculated from all changed flows. Predilution also lowers the solute concentration entering the filter and therefore reduces clearance to some extent; a dilution factor can estimate this effect. FF is generally lower with CVVHD at comparable net fluid removal because diffusive clearance does not require replacement-fluid ultrafiltration. Observational and quasi-randomized data suggest that CVVHD may provide longer filter life than CVVH with prefilter replacement fluid.

Postfilter Hematocrit as an Alternative Index

Although FF is the traditional index used to describe the effect of hemoconcentration on the risk of filter clotting, postfilter hematocrit has recently been proposed as an alternative measure for predicting clotting risk. However, the available data establishing the superiority of either index over the other remain limited.

Reassessment of CKRT Dose

Although delivery of 20–25 mL/kg/h is appropriate for most patients treated with CKRT under most circumstances, the dose should be reassessed frequently because critical illness changes dynamically over time. In some situations, doses above 25 mL/kg/h may become necessary. Examples include:

Rhabdomyolysis

Tumor lysis syndrome. In these situations, the reduction in potassium clearance caused by AKI is exacerbated by the release of very large amounts of potassium into the

circulation, and CKRT doses exceeding 40 mL/kg/h may be required to maintain metabolic control. [14]

Combining IHD and CKRT in Severe Hyperkalemia

In these situations, it may be necessary initially to take advantage of the high instantaneous clearance of IHD to rapidly correct life-threatening hyperkalemia, followed immediately by CKRT to provide a continuous and higher total daily clearance dose in order to maintain metabolic control. When high CKRT doses are used, once metabolic control is achieved and the underlying disease process improves, the dose should be reduced gradually toward the standard range. The aim is to avoid excessive removal of:

Phosphate

Micronutrients

Drugs.

When Is High-Dose CKRT Used in Lactic Acidosis?

One situation in which high-dose CKRT should not be used routinely, despite ongoing debate, is the treatment of lactic acidosis, particularly type A lactic acidosis, that is, acidosis resulting from shock or organ-specific hypoperfusion.

Although lactate is a small, water-soluble molecule and can therefore be removed relatively easily by dialysis, with S ≈ 1, dialysis treatment generally has a very limited effect on serum lactate levels. This is because the clearance provided by CKRT, even at very high doses such as 50 mL/min, remains extremely low compared with normal endogenous lactate clearance. Endogenous lactate clearance in critically ill patients has been estimated at approximately 750–2000 mL/min. Consequently, CKRT usually has only a small effect on serum lactate levels, and changes in lactate levels in patients receiving CKRT can therefore generally be interpreted in much the same way as in patients not receiving CKRT. [8, 15]

Type B Lactic Acidosis

Although it is less common, dialysis treatment plays an important role in treating type B lactic acidosis caused by drug toxicity, such as metformin poisoning. In this situation, however, intermittent hemodialysis (IHD) is often preferred over CKRT because of its ability to achieve higher clearance.

Blood Flow

Compared with intermittent hemodialysis (IHD), the usual range of blood flow rates, Qb, used in continuous kidney replacement therapy (CKRT) is much lower. As noted previously, Qb usually has very little effect on the CKRT dose within the usual dose range. However, when high CKRT doses are used, Qb may begin to influence clearance; in these situations, an adequate Qb relative to Qd or Qr,pre is required to maintain highly efficient solute removal.

Apart from this, maintaining an appropriate Qb is necessary to prevent hemofilter clotting. Although increasing Qb will always mathematically reduce the filtration fraction, the potential benefit for prolonging filter life begins to diminish with further increases in Qb, most likely when it exceeds approximately 250 mL/min.

For example, one trial randomized 100 patients receiving CKRT either without anticoagulation or with heparin to a blood flow rate of 150 mL/min or 250 mL/min, and found no difference in filter life between the groups. This may be because increasing Qb in a circuit with fixed resistance also increases the risk of pressure alarms. These pressure alarms cause the blood pump to stop or slow down, which may promote filter clotting if it occurs repeatedly.

Blood Flow (Qb) during Citrate Anticoagulation (RCA)

When citrate is used for anticoagulation (Regional Citrate Anticoagulation), a lower blood flow rate, such as 120–150 mL/min, is generally recommended. There are two main reasons for this:

Reducing Qb decreases the amount of citrate needed to maintain adequate anticoagulation and therefore reduces the risk of metabolic complications associated with RCA.

RCA is sufficiently effective to maintain filter patency even when a relatively low Qb is used.

Constructing a CKRT Prescription

Prescription item	Required documentation
Indication and modality	Reason for initiation; selection of CVVHD, CVVH, or CVVHDF; need for continuous support
Weight and flows	Weight used; Qb; Qd; prefilter and postfilter replacement; units
Dose	Qeff and nominal dose; method of predilution correction when used; target delivered dose
Fluids Fluid removal	UFnet; patient fluid-balance target; criteria for reducing or stopping removal
Solutions	Full composition; compatibility of solutions with RCA; additional infusions and how they are accounted for
Anticoagulation	Strategy; targets; infusion and sampling sites; plan for circuit interruption
Monitoring	Electrolytes, blood gases, and calcium during RCA; pressures and interruptions; timing of reassessment
Recovery and review	Indicators for a trial of discontinuation or transition; review of medications and nutrition according to the delivered dose

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Complications

Continuous kidney replacement therapy (CKRT) provides a means of controlling fluids and solutes in critically ill patients, but exposes them to risks involving interactions among illness severity, vascular access, the extracorporeal circuit, anticoagulation, and solution composition. Correcting a laboratory result or clearing a machine alarm is therefore insufficient; the underlying mechanism must be identified, its effect on the patient assessed, and treatment then adjusted and the response monitored. Complications include catheter injuries, circuit failure, bleeding, disturbances of temperature, hemodynamics, electrolytes, and acid–base balance, and unintended removal of drugs and nutrients. [1,2,3]

Clinical framework and level of evidence

The recommendations in this chapter are based on final guidelines, followed by randomized trials, and then observational studies, reviews, and consensus statements. In October 2026, the KDIGO 2026 update on acute kidney injury and acute kidney disease remained a draft being prepared for final publication after public consultation had closed; it is not treated here as a final guideline. The KDIGO 2012 guidelines are cited because they are the available final reference for this topic, with subsequent evidence used to update issues that have evolved. Operational matters, such as measurement frequency and pump adjustment, require an approved unit protocol compatible with the machine and solutions used. [4,5]

Vascular access complications

Mechanical injuries and prevention

Insertion of a dialysis catheter may be associated with arterial puncture, bleeding or hematoma, pneumothorax or hemothorax depending on the insertion site, malposition, or air embolism. Site selection must balance blood flow, ease of care, infection and thrombosis risks, and preservation of vessels required for future dialysis. KDIGO suggests starting with the right internal jugular vein when suitable and avoiding the subclavian site whenever possible because of the risk of venous stenosis. [3,4]

The guidelines recommend ultrasound guidance by a trained practitioner, asepsis and maximal sterile barrier precautions, and documentation of catheter position and verification of readiness for use according to the insertion site and unit protocol. Absence of resistance when flushing the catheter alone must not be interpreted as evidence that the required blood flow can be achieved throughout treatment. [4,6]

Catheter dysfunction and recirculation

Reduced actual flow may result from kinked tubing, contact between the catheter tip and the vessel wall, catheter malposition, or a thrombus within or around the catheter. Repeated pump interruptions cause blood stasis, reduce actual treatment hours, and may shorten filter life. Management of recurrent clotting therefore begins with examining the access, tubing, and pressure trends before automatically increasing anticoagulation. [1,7]

Highly negative access pressures indicate resistance in the line withdrawing blood from the patient, whereas increased return pressure may indicate resistance in the line returning blood to the patient; readings are affected by flow and by the positions of the patient and machine. Reversing the access and return lines can temporarily improve flow but may increase recirculation, and is therefore not a permanent solution to catheter dysfunction. The change is documented and the need for catheter repositioning or replacement assessed. [7]

Bloodstream infection and thrombosis

Prevention includes hand hygiene, disinfection of connections, insertion-site and dressing care, minimizing unnecessary manipulation, and daily review of the need for the catheter. The CDC does not recommend routine replacement of central or dialysis catheters solely to prevent infection.

When catheter-related bloodstream infection (CRBSI) is suspected, cultures are obtained and other sources investigated. Catheter removal or replacement is decided according to illness severity, the organism, and complications; the catheter is not removed on the basis of fever alone. [6]

Catheter-related venous thrombosis may present with limb or neck edema or impaired flow, or may be asymptomatic. Appropriate imaging is used to confirm the diagnosis when suspected, and management is individualized according to bleeding risk, the need for the catheter, and the thrombosis site. Venous or catheter thrombosis must not be confused with filter clotting, because each requires a different assessment and management approach. [2,3]

Circuit and filter complications

Clotting, Membrane Fouling, and Reduced Permeability

Circuit stoppage and the need for unplanned replacement interrupt clearance, reduce the delivered dose, cause blood loss if blood cannot be returned, and increase filter consumption and nursing workload. Modifiable factors include low blood flow, repeated alarms, catheter dysfunction, inadequate anticoagulation, and hemoconcentration within the filter.

Postdilution CVVH increases the importance of the filtration fraction, whereas prefilter replacement (predilution) reduces hemoconcentration but may lower actual clearance. [2,7]

An increase in transmembrane pressure (TMP) is not synonymous with clotting. It may rise because of protein deposition and reduced membrane permeability (membrane fouling), a change in flow, or obstruction of the effluent pathway. An increased pressure drop across the blood compartment of the filter (filter pressure drop), however, may support the presence of increasing blood-flow resistance. Serial trends are interpreted together, and pressure definitions and the method by which the machine calculates them are reviewed. [7]

Problem	Expected pattern	Initial review
Access dysfunction	More negative access pressure or increased return pressure; position-related alarms	Catheter, kinks, tip position, actual flow
Reduced membrane permeability due to deposits (membrane fouling)	Gradual rise in TMP; the blood-side pressure drop may not rise to the same extent	Pressure trends, effluent, membrane permeability
Circuit clotting	Increasing blood-flow resistance or visible clots; TMP may also rise	Pump stoppages, anticoagulation, hemoconcentration, and filtration fraction

Blood loss and thrombocytopenia

When blood cannot be returned from the circuit, blood loss is estimated from the blood volume within the specific tubing set and filter; a uniform volume must not be assumed for all machines. This loss is added to clinical bleeding and repeated blood sampling when interpreting anemia. The contents of a clotted circuit must not be returned, and no attempt must be made to push clots into the patient; the safe-return requirements specific to the machine and unit are followed. [2]

Although the relationship between CKRT and thrombocytopenia has been recognized clinically for years, recent observational data have reaffirmed an association between CKRT and reduced platelet counts in patients receiving it. Platelet count decreases of approximately 33%–50% from baseline have been described in some observational studies. This is not an expected range for every patient, and a fall of this magnitude is not automatically mild; the clinical context, including sepsis, coagulopathy, drugs and HIT after heparin exposure, must be assessed. (Griffin BR, et al. Crit Care Med. 2021;49:e130–e139. doi:10.1097/CCM.0000000000004763.) Given the many possible causes of thrombocytopenia in critically ill patients, CKRT should be considered a cause only after other causes have been excluded.

The differential diagnosis includes sepsis, disseminated intravascular coagulation (DIC), drugs, dilution, other devices, and heparin-induced thrombocytopenia (HIT). The previous count, magnitude and timing of the decrease, presence of new thrombosis, and exposure to all sources of heparin are reviewed. [2,8]

Hemolysis and acute reactions

Hemolysis should be considered when there is an unexplained increase in potassium, a decrease in hemoglobin accompanied by elevated LDH and reduced haptoglobin, or a change in plasma color. The lines are examined for kinking, obstruction, and mechanical problems, and other causes, including associated devices, are reviewed.

Very important: If hemolysis within the circuit is suspected, treatment is stopped and the patient is assessed immediately. Blood suspected of being hemolyzed must not be returned because of the risk of loading the patient with potassium. This safety rule is derived from the dialysis-emergency literature and must be applied together with the local CKRT protocol. [9]

Allergic reactions to the membrane or tubing may present as sudden hypotension, bronchospasm, or a rash after treatment starts. Air can also enter when connections are exposed or become disconnected, despite the presence of air detectors. If a severe reaction or air embolism is suspected,

blood pumping is stopped, the circuit is secured, and the emergency response is initiated according to the unit protocol. Alarm systems or air detectors must not be bypassed in order to continue treatment. [3,9]

Hemodynamic and thermal disturbances

Hypotension and net ultrafiltration

CKRT does not prevent hypotension. It may be caused by fluid removal exceeding the capacity for plasma refilling, bleeding, septic vasodilation, cardiac failure, or an arrhythmia. The response therefore requires assessment of both the patient and the circuit; not every episode of hypotension may be attributed to CKRT, nor should fluids be administered automatically. [3,10]

When perfusion deteriorates, net ultrafiltration (UFnet) can be reduced or fluid removal temporarily stopped while solute clearance is continued if possible, until the cause is treated and the plan reassessed. The decision depends on blood pressure, trends in vasopressor doses, congestion, cardiac output, and perfusion, rather than on the fluid-balance target alone. [10]

High UFnet rates are associated with worse outcomes in some observational analyses, but this association neither defines a uniform safe threshold nor establishes causality. Fluid accumulation may also be harmful. A graduated prescription is needed that balances decongestion against hemodynamic tolerance, with reassessment when the condition, intake, or machine operating time changes. [10]

Hypothermia

The patient loses heat as blood passes outside the body and exchanges heat with fluids. In a retrospective observational study of 300 patients, hypothermia, defined as a time-weighted mean below 36 degrees Celsius, occurred in 23.7% during the first 24 hours; this proportion is specific to that cohort and is not a fixed incidence rate. Its association with mortality does not establish that it is the cause. [11]

Temperature is included in monitoring, and approved warming systems are used when needed, with the response monitored. Cooling may mask fever, so its absence does not exclude sepsis. The patient’s temperature is reviewed before and during treatment and after changes in flow or warming measures. [11]

Anticoagulation complications

Heparin and Heparin-Induced Thrombocytopenia (HIT)

Systemic heparin increases bleeding risk and may cause HIT.

KDIGO 2012 suggests regional citrate anticoagulation (RCA) rather than heparin during CKRT in patients without contraindications to citrate (as discussed in detail previously). [4]

When HIT is suspected, the 4Ts score is used to estimate probability, followed by appropriate testing. ASH recommends stopping heparin when the probability is intermediate or high and selecting a non-heparin anticoagulant according to bleeding risk and the indication. RCA alone is insufficient to treat the risk of systemic thrombosis in acute HIT because its effect is primarily on the circuit; a hematologist must participate in management when needed. The cited ASH guidelines were published in 2018 and remain a specialist reference for this issue. [8]

Citrate-related disorders

Accumulation versus alkali overload

RCA binds ionized calcium within the circuit and reduces clotting, while the patient requires calcium replacement. Metabolism of the citrate reaching the patient can generate an alkali load; metabolism of one millimole of trisodium citrate is equivalent to approximately three millimoles of bicarbonate, but the net effect depends on solution composition and the removal of citrate and bicarbonate. [13]

Citrate accumulation is considered the most concerning complication of RCA and is also called citrate toxicity or citrate lock. It develops when the citrate amount exceeds the capacity to metabolize it, resulting in accumulation of citrate–calcium complexes. Citrate or buffer overload, by contrast, occurs with preserved metabolism and an excessive alkali load.

There is a third pattern: insufficient buffer delivery, characterized by persistent acidosis without evidence of accumulation. This distinction is essential because increasing citrate removal may help in accumulation or alkalosis but may worsen the third pattern. [13]

Parameter	Citrate accumulation	Buffer overload	Insufficient buffer delivery
Mechanism	Insufficient metabolism	Preserved metabolism and excessive alkali load	Insufficient alkali load
tCa/iCa ratio	Tends to rise; 2.5 or more supports suspicion	Usually not elevated	Usually not elevated
Systemic calcium and its replacement	iCa may fall and replacement requirements increase	Usually no escalating requirement	Usually no escalating requirement
Acid–base balance	Acidosis or a mixed disorder	Metabolic alkalosis	Persistent acidosis
Management approach	Reduce the load and increase removal; stop RCA if it persists	Review citrate, bicarbonate, and removal	Review clearance and administer buffer after excluding accumulation

Diagnosis and monitoring

The total-to-ionized calcium ratio (tCa/iCa) is calculated using identical units. Total calcium in mg/dL must not be divided directly by iCa in mmol/L. To convert total calcium to mmol/L, divide its value in mg/dL by approximately 4.01.

Teaching example: 10 mg/dL is equivalent to approximately 2.49 mmol/L; if iCa is 1.00 mmol/L, the ratio is approximately 2.49, not 10. [13]

A serial rise in the ratio to 2.5 or more supports suspicion of accumulation, particularly when accompanied by reduced systemic iCa, escalating calcium replacement, and worsening acidosis. An isolated value is insufficient, and a mixed disorder may mask a change in pH. Albumin correction of calcium is not automatically used to calculate the ratio; recent consensus acknowledges that the effect of this correction remains disputed. [14]

Systemic iCa is measured in a sample representative of the patient, avoiding contamination by the calcium infusion, whereas postfilter iCa is measured at its designated sampling site to monitor anticoagulation. The usual postfilter range is 0.25-0.35 mmol/L, but the target depends on the protocol and the accuracy of the blood gas analyzer at low concentrations. Monitoring is intensified at initiation and after dose adjustments or hemodynamic changes, and total calcium is measured periodically; no single frequency has been established for all situations. [14]

Risk factors and management

When accumulation is suspected, the citrate dose reaching the patient and calcium replacement are reviewed, perfusion is addressed, the load is reduced in a manner consistent with the coupling of blood flow and the citrate pump, and citrate removal is increased when appropriate. If the disturbance persists despite adjustment, RCA is stopped and an alternative strategy selected while appropriate kidney replacement therapy continues. Increasing calcium alone is insufficient; increasing clearance also requires review of drug doses and electrolyte losses. [14]

Alkalosis with a stable ratio and no escalating calcium requirement, however, prompts review of the total alkali load, bicarbonate concentration, and the blood-flow-to-effluent ratio. In persistent acidosis, inadequate delivered dose, lactate and ketones, and insufficient buffer delivery are investigated before assuming citrate accumulation. A single pump must not be adjusted in isolation from the rest of the RCA prescription. [13]

Practical flowchart for managing citrate accumulation:

Citrate accumulation

Ci-Ca CVVHD · protocol-specific decisions

1. Assess

Check routinely and if clinically suspected, including hypoxia during resuscitation. Indicators: a marked fall in ionized calcium, total calcium > 3 mmol/L, or a total/ionized calcium ratio > 2.5. If clinically significant accumulation is absent, continue treatment.

2. Lower citrate delivery

If accumulation is present, reduce the citrate dose; a postfilter calcium target of 0.4–0.5 mmol/L may be accepted in this protocol. Reassess. If accumulation resolves, proceed to stage 4.

3. If accumulation persists

Reduce blood flow to lower systemic citrate delivery. At a dialysate flow of 1500 mL/h, do not reduce blood flow below 60 mL/min. Reassess: if accumulation persists, stop Ci-Ca treatment; otherwise proceed to stage 4.

4. Review acid–base status

If reduced citrate delivery has caused metabolic acidosis, correct it with bicarbonate. Continue Ci-Ca treatment with close monitoring, whether or not bicarbonate was required.

Fresenius Medical Care · Ci-Ca CVVHD brochure, p. 27. Use the applicable device instructions and local protocol.
www.linkedin.com/in/alhariri-mahmoud

Illustrative management options for citrate accumulation in the manufacturer-described Ci-Ca CVVHD protocol. The flow limits and calcium targets shown are specific to that protocol and require the corresponding device instructions.

Electrolyte and acid–base disorders

Hypophosphatemia

CKRT can continuously remove phosphate as it redistributes from cells; initial hyperphosphatemia may therefore turn into hypophosphatemia during treatment.

The higher risk of hypophosphatemia with CKRT than with IHD is related to the kinetics of phosphate movement between body compartments (intercompartmental kinetics). Most total-body phosphorus is stored in bone and teeth. Of the nonosseous pool, much is intracellular and incorporated into organic compounds, unlike potassium, which is mainly a free intracellular ion. Redistribution to extracellular fluid can limit phosphate removal during a short dialysis treatment.

Because of these slow kinetics, treatment duration is the principal determinant of the amount of phosphate removed by KRT. Although IHD efficiently removes phosphate from the extracellular compartment, a single IHD session removes only a modest amount of the body's total phosphate stores. The continuous nature of CKRT overcomes slow phosphate redistribution between compartments. Hypophosphatemia may appear within approximately 48 hours when phosphate-free solutions are used, but it can occur earlier or later depending on stores, nutrition, delivered dose and redistribution. Phosphate monitoring therefore begins when CKRT starts; it should not be deferred until 48 hours have elapsed. (Heung M, Mueller BA. Semin Dial. 2018;31:213–218. doi:10.1111/sdi.12677.)

Severe deficiency may cause respiratory muscle weakness, rhabdomyolysis, and cardiac dysfunction. Delayed weaning from ventilation cannot be explained by phosphate alone, but it is a correctable factor. [15]

A meta-analysis published in 2025 found no clear statistical association between hypophosphatemia during CKRT and mortality, but found an association with longer ventilation duration and intensive care stay. These relationships are based on heterogeneous observational studies and therefore establish neither causality nor that replacement improves survival. [16]

The Korean guidelines designated for 2025 and published in 2026 suggest using phosphate-containing solutions to prevent deficiency, with a conditional recommendation and very low-certainty evidence. The full composition of the solution, including potassium, glucose, and calcium, is reviewed, and it is not used in persistent hyperphosphatemia without assessment. Enteral or intravenous replacement may be used according to severity, but

adding phosphate to bags requires an approved pharmaceutical procedure to verify compatibility, sterility, and concentration; it must not be improvised at the bedside. [17]

Potassium, magnesium, and calcium

The potassium concentration in dialysate and replacement solutions is selected according to the current value and its trend, not solely the result at treatment initiation. Continuing potassium-free fluids after hyperkalemia has been corrected may cause hypokalemia, particularly with insulin. Conversely, persistent hyperkalemia requires review of interruptions, flow, and dose, as well as tissue breakdown or hemolysis. [15]

Magnesium may decrease because of removal, which is exacerbated by its chelation by citrate. Its concentration is reviewed in arrhythmia or hypokalemia refractory to replacement. Calcium replacement during RCA is adjusted on the basis of systemic iCa, with the sampling site and pump checked before responding to an unexpected value. [15]

Sodium and osmolality

A standard CKRT solution may correct a sodium disorder at an undesirably rapid rate, particularly in chronic hyponatremia, or lower sodium in a patient in whom therapeutic hypernatremia is being maintained because of brain injury. The correction plan is defined before treatment starts, and the effects of additional fluids, citrate solution, nutrition, and urine are calculated. Any customization of solutions requires pharmaceutical supervision, a plan for repeated measurements, and documentation of the actual concentration. [7,18]

The calculated sodium concentration in the solution is not equivalent to the patient’s blood sodium after one hour; the latter is affected by body water and changes in intake and output. Recovery of urine output may also accelerate correction of hyponatremia even without changing the machine. The plan is adjusted according to serial measurements, and the mixing equation alone must not be relied upon. [18]

Glucose and ketones

CKRT affects glucose balance according to its content in the fluids, the blood concentration, and the dose. Some commercial phosphate-containing solutions are glucose-free; this must not be generalized to all preparations. Nutrition and glucose and insulin infusions are reviewed together, especially when feeding is interrupted or machine operation changes. [19]

A series of eight cases was described in critically ill patients with diabetes who developed ketosis without elevated glucose while receiving a glucose-free CKRT solution. Anion-gap acidosis worsened despite improvement in lactate, and ketones improved after increasing energy and dextrose provision with appropriate insulin. This is evidence from a case series; it neither determines an incidence rate nor establishes that the solution alone was the cause. [19]

In unexplained high-anion-gap acidosis, β-hydroxybutyrate is measured and lactate, citrate, delivered dose, and the medication and nutritional context are reviewed. Normal glucose does not exclude euglycemic ketoacidosis. Treatment is individualized according to the cause, with monitoring of potassium and glucose and avoidance of unaccounted-for fluid loading. [19]

Nutrient losses and drug removal

Membranes do not distinguish between molecules intended for removal and beneficial molecules able to pass through them. Studies have documented losses of amino acids and micronutrients during kidney replacement therapy, varying with modality, dose, membrane, and nutritional status. A range of 10-20 grams of amino acids per day is cited as an approximation, not as a fixed amount to be added mathematically to every patient’s requirements. [20,21]

Inadequate drug exposure or toxicity may also result from an inappropriate prescription, a change in residual clearance, or treatment interruption. Drug and nutrient losses are part of CKRT safety and are reviewed within the daily care plan detailed in the next section. Observing the loss of a substance in the effluent does not establish that replacing it at high doses improves outcomes. [21,22]

Monitoring and early response

Measurement frequency is individualized according to stability, the risk of disturbances, and anticoagulation, and is intensified after treatment initiation or prescription changes. The following table is an organizational framework derived from the mechanisms of complications, not a dosing protocol or a uniform mandatory measurement schedule. [2,7,14,15]

Domain	What to monitor	Escalation trigger
Hemodynamics	Blood pressure, perfusion, vasopressors, UFnet	Deteriorating perfusion or intolerance of fluid removal
Circuit	Flow, pressure trends, alarms, hours of interruption	Clots, repeated alarms, unplanned circuit loss
RCA	Systemic and postfilter iCa, tCa/iCa, calcium replacement, pH	Rising ratio with reduced iCa or increased replacement
Electrolytes	Sodium, potassium, phosphate, magnesium	Rapid change, severe deficiency, arrhythmia
Metabolism	Glucose, lactate, ketones when indicated	Unexplained acidosis or low glucose
Safety	Temperature, bleeding, platelets, catheter site	Acute reaction, hemolysis, suspected infection or HIT

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Multidisciplinary Care

Caring for a patient receiving CKRT requires integrating the dialysis prescription with the management of critical illness, nutrition, medications, mobility, and the patient's goals. Stable readings on the machine do not necessarily mean that the prescribed dose has been delivered in full, and a decrease in urea does not demonstrate that antibiotic doses are appropriate or that the fluid balance target has been achieved. Care rests on clearly defined responsibilities, communication when treatment changes, and regular review of what was prescribed and what was actually achieved. [1, 2]

Team Organization and Responsibilities

The Korean guidelines suggest a specialized or multidisciplinary approach to improve filter life and reduce downtime. This recommendation is based on expert consensus and retrospective studies; no randomized evidence demonstrates that establishing the team alone reduces mortality. The structure is tailored to the institution's resources while retaining expertise in nephrology, critical care, nursing, pharmacy, nutrition, and rehabilitation. [2]

Team member	Main responsibility	Coordination point
Nephrology	Indication, modality, clearance, anticoagulation, recovery	Reassessment of the need for treatment, prescription, and access
Critical care	Perfusion, congestion, and management of critical illness	Fluid target, tolerance of removal, and procedures
Nursing	Operation, measurements, alarms, and documentation of treatment actually delivered	Reporting changes, downtime, and circuit loss
Pharmacy	Dosing, TDM, solution compatibility	Every change in clearance, downtime, or modality

Team member	Main responsibility	Coordination point
Dietetics	Energy, protein, and micronutrients	Actual intake, treatment-related losses, and tolerance of nutrition
Rehabilitation	Graded mobilization and protection of lines	Patient stability and securing the catheter and circuit

This is a practical allocation of responsibilities, not an organizational model tested as a single package in a randomized trial. The unit should specify who has the authority to change the prescription, who may adjust UFnet within written limits, and when medical review is required. Instructions are documented so that fluid balance goals do not conflict with circulatory safety. [2, 3]

Daily CKRT Prescription Review

The prescription is reviewed daily and whenever there is a significant change in circulation, electrolytes, urine output, or medications. KDIGO recommends measuring and reviewing the dose actually delivered; the prescription alone does not describe the clearance the patient received. The following table outlines the items to review, based on established prescription components. [4, 5]

Item	Clinical question
Indication	Does the indication for CKRT persist, and are its goals defined?
Modality	Does CVVH, CVVHD, or CVVHDF achieve the current goals?
Dose	What was prescribed, and what was achieved after accounting for downtime and predilution?
Fluid balance	What is the patient’s overall target, and what UFnet is required within the patient’s tolerance?
Access and filter	Is flow stable, and what is causing alarms or a short filter life?

Item	Clinical question
Anticoagulation	Is the target achieved, and are there signs of bleeding or a metabolic disturbance?
Solutions	Is the sodium, potassium, phosphate, and base composition appropriate?
Drugs	Has the actual dose or residual function changed, and is TDM required?
Nutrition and mobility	What intake was actually delivered, and can nutrition be increased and rehabilitation advanced?
Recovery	Has kidney function improved sufficiently to allow a trial of discontinuation or transition to another modality?

Patient Balance Versus Machine Removal

The UFnet recorded by the machine differs from the patient's overall fluid balance. The patient's balance includes medications, nutrition, blood products, urine, drains, and all other inputs and outputs; citrate and calcium fluids are also reconciled with the machine's accounting method to avoid double recording or omission. [3]

Example:

If external intake is 3000 mL/day, outputs outside the machine are 500 mL/day, and the target is a negative balance of 1000 mL, the required removal through CKRT is 3500 mL/day. This corresponds to approximately 146 mL/hour when treatment runs for 24 hours, or 175 mL/hour if it is limited to 20 hours. The calculation does not mean that the latter rate is hemodynamically tolerated; the target, intake, or treatment delivery plan must be adjusted according to the patient's stability. [3]

Pharmacokinetics and Drug Dosing

Determinants of Clearance

Total clearance is understood as the sum of residual kidney clearance, nonrenal clearance, and clearance through the extracorporeal circuit. These components change with recovery and illness severity. Drug removal is affected by molecular weight, the unbound fraction, volume of distribution (Vd), the membrane, modality and flow, and adsorption. The creatinine value during CKRT is insufficient to estimate residual kidney function or the drug dose. [6, 7]

In convective filtration, clearance is approximated by multiplying the sieving coefficient (SC) by the filtration rate, accounting for predilution. In diffusive dialysis, CVVHD, the approximation depends on the saturation coefficient and the relevant flow. CVVHDF combines two overlapping mechanisms, and independent estimates must not be added in a way that assumes there is no overlap. Effluent alone also does not capture adsorption onto the membrane. [7]

Loading and Maintenance Doses

The loading dose is primarily related to the volume of distribution and target concentration, whereas the maintenance dose is related to clearance.

Therefore, AKI or CKRT does not automatically imply a reduction in the loading dose. Sepsis and fluid resuscitation may increase the volume of distribution of hydrophilic drugs, requiring appropriate loading to achieve early exposure; this is individualized according to the drug, weight, infection, and clinical context. [7]

The phrase “dose for a patient on CKRT” does not represent a fixed category! Alongside the recommendation, document the drug name and indication, modality, actual effluent, dosing weight, residual function, downtime, and the timing of a new filter. Review is repeated when urine output returns, the modality changes, or CKRT stops, because continuing the previous dose may cause underexposure or accumulation. [6]

Antibiotics and Therapeutic Drug Monitoring (TDM)

Prompt administration of appropriate empirical therapy should be combined with individualized maintenance dosing according to changing clearance. Therapeutic Drug Monitoring (TDM) helps detect underexposure and toxicity; however, it requires documentation of dose and sample timing, downtime, the infusion method, and the pharmacokinetic/pharmacodynamic (PK/PD) target. A concentration value must not be interpreted without this information. [8]

The findings of the Conference Report and Expert Panel published on 07.05.2020 recommend TDM for several antibiotics in critically ill patients, including vancomycin, aminoglycosides, beta-lactams, and linezolid when measurement is available. These are expert recommendations supported by drug exposure data; they do not mean that TDM has been shown to reduce mortality for every drug or every CKRT population. [8]

For vancomycin in serious invasive MRSA infections, the American consensus guidelines recommend targeting a 24-hour area under the curve (AUC) between 400 and 600 mg·h/L when the assumed MIC is 1 mg/L. This target is not generalized to every use of vancomycin, and the estimation method during CKRT must account for changing clearance and appropriate measurements. The reference was published in 2020 and remains listed as the current guideline on the IDSA website. [9]

Prolonged or continuous infusion of beta-lactams may help maintain exposure above the MIC after an appropriate loading dose and review of formulation stability and intravenous compatibility. The BLING III trial did not achieve a statistically significant difference in 90-day mortality in its primary analysis, although clinical cure improved.

However, the contemporaneous meta-analysis pooling randomized trials found lower 90-day mortality with prolonged infusion, with a risk ratio of 0.86 and a 95% credible interval from 0.72 to 0.98. This is evidence in sepsis and septic shock generally and does not specify a CKRT-specific dose; the infusion method is therefore selected together with the pharmacist and does not replace dose adjustment or measurement when available. [10, 11]

Clinical Nutrition

Assessment and Energy

Prior nutritional status, actual intake, the severity of catabolism, interrupted feeding, and fluid retention are reviewed. The phrase “renal nutrition” is insufficient to identify the appropriate formulation, because CKRT may allow protein and electrolyte intake that differs from the needs of a stable patient on chronic dialysis.

Enteral nutrition is selected when appropriate, and parenteral nutrition is considered if requirements cannot be met, according to the critical care context. [12]

Energy is estimated individually, with measurement by indirect calorimetry preferred when appropriate and available. Nonnutritional calories from glucose, metabolized citrate, and drugs such as propofol are included, bearing in mind that exposure to them changes as the prescription changes. It must not be assumed that all infused citrate reaches the patient or is converted to energy, because some of it is removed. [12, 13]

Protein and the EFFORT Study

For critically ill patients with AKI, AKI on CKD, or kidney failure receiving CKRT or PIKRT, ESPEN 2024 suggests a protein intake of 1.5 g/kg/day, which may be increased to 1.7 g/kg/day. The recommendation for this range is grade 0 and based on expert consensus; it is not the result of a trial establishing the best value for all patients. Usual weight or preadmission weight is preferred when available, and a weight affected by fluid overload is not used directly to calculate requirements. [12]

In the EFFORT Protein trial, targeting higher protein doses did not improve the time to discharge alive from hospital, and the findings suggested possible harm in some patients with AKI. The post hoc analysis of patients with AKI calls for caution; however, it does not demonstrate that the range recommended by ESPEN is harmful, nor does it define an optimal dose for every patient receiving CKRT. A very high target is not adopted for all patients merely because losses occur in the effluent. [14, 15]

The amount of protein actually delivered, urea, gastrointestinal tolerance, electrolytes, and the course of catabolism are monitored.

Calculation example for the ESPEN recommendation: a usual weight of 70 kg gives 105 g/day at 1.5 g/kg and 119 g/day at 1.7 g/kg. Estimated amino acid losses are not automatically added again on top of this target, because this could lead to double counting. [12]

Vitamins and Trace Elements

Studies have documented changes in amino acids, water-soluble vitamins, and some trace elements during AKI and dialysis treatment. Inflammation, intake, and distribution between tissues have also been shown to alter concentrations, so a low plasma value does not always reflect a deficit that can be corrected with the same dose. [16, 17, 18]

Usual provision and deficiency risks are reviewed in malnutrition or prolonged CKRT, and targeted measurements are requested when they would change the clinical decision. There is insufficient evidence for a uniform supraphysiological supplementation regimen for all elements in all patients, and measuring the loss of an element is insufficient to establish the benefit of high doses of that element.

The 2021 scoping review and older physiological studies are used here to describe losses, not to establish a definitive treatment strategy. [17, 18]

Refeeding

The risk of refeeding syndrome is assessed when intake has been interrupted or in malnutrition, because decreases in phosphate, potassium, and magnesium may coincide with CKRT-related losses.

Nutrition is increased in a carefully planned manner, electrolytes and intake are monitored, and replacement is coordinated between nutrition, pharmacy, and nephrology. A high risk of deficiency may require adjustment of CKRT solutions alongside the nutrition plan. [13]

Mobilization and Physical Rehabilitation

CKRT is not an absolute contraindication to mobilization, but the decision depends on hemodynamic and respiratory stability, consciousness, bleeding, and catheter and circuit integrity. A systematic review found that rehabilitation and early bedside mobilization were feasible in selected patients, with limited overall quality and variation in event reporting and levels of mobility. The finding should therefore not be interpreted as a guarantee of the safety of every activity. [19]

Activity progresses from passive movement to active participation, sitting, or suitable activity according to the team's assessment. A designated team member protects the catheter and lines during movement, and their lengths and securement, the machine's position, and alarms are reviewed. Activity is stopped if intolerance develops or there is a risk of catheter dislodgement or circuit disconnection. These measures remain dependent on the patient's condition and the team's experience, and no single mobilization protocol suits all patients. [19]

Transition, Recovery, and Communication

The return of urine output, kidney clearance when measurable, ongoing fluid and electrolyte requirements, and the possibility of transition to PIKRT or IHD or a trial of discontinuation are reviewed.

KDIGO recommends discontinuing dialysis treatment when kidney function becomes sufficient to meet the patient's needs or when treatment is no longer consistent with the goals of care. An isolated urine output measurement or a low creatinine value while on the machine does not demonstrate sufficient recovery. [4]

When CKRT stops or the patient transitions to another modality, a plan for medications, electrolytes, nutrition, fluids, and anticoagulation is handed over, with documentation of when the last circuit stopped and the most recent measurement results. The explanation to the patient or their representatives includes the goals of support, what has been achieved, and what remains uncertain, without using filter life as a substitute for patient outcomes. This information helps the team continuing the patient's care adjust treatment after the transition. [4, 2, 6]

Quality Assurance and Performance Indicators

Structure, Care Processes, and Outcomes

Structure includes training, the availability of staff, solutions, and measurements, and the capacity to maintain machines. Care processes include dose prescription, recording downtime, alarm management, monitoring, and communication. Outcomes include patient safety, achievement of treatment goals, recovery, and clinical outcomes. CKRT indicators have been developed through reviews and Delphi consensus, and there are no universally validated thresholds for every indicator. The foundational 2018 reference predates recent clinical evidence and is used for the methodological framework. [20]

Operational CKRT Dashboard

The following table is a practical proposal based on the quality indicator framework, with operational definitions that must be established locally. Not all indicators are valid measures for comparisons between institutions without standardizing definitions and adjusting for differences between patients. [20]

Indicator	Proposed definition — Operational definition	Use — Interpretation
Delivered effluent dose	Actual effluent volume over 24 hours ÷ calculation weight ÷ 24; the dilution-corrected clearance estimate is recorded separately	Detecting the difference between the prescribed and actually delivered dose
Downtime	Hours of treatment interruption and the reason for each interruption during the day	Distinguishing malfunctions, clotting, transport, and procedures
Filter life	Actual operating hours for each filter and the reason its use ended	Evaluating access, anticoagulation, and operation
Unplanned circuit loss	Number of unplanned circuit replacements divided by the number of treatment days, with documentation of the reason for replacement	Estimating burden and preventable blood loss

Indicator	Proposed definition — Operational definition	Use — Interpretation
Achievement of UFnet	Achieved removal compared with the target, together with the patient’s balance	Assessing fluid control within tolerance
RCA events	Low iCa, an elevated ratio, and alkalosis according to the unit’s definitions	Monitoring metabolic safety
Bleeding	Bleeding events using a standardized definition, their severity, and transfusion	Assessing anticoagulation safety
Electrolytes and temperature	Deficiency or hypothermia events relative to the number of treatment days or patients, with a fixed denominator	Measuring the impact of prevention protocols
Drug exposure	Attainment of the TDM target when requested, with documentation of sample timing	Monitoring dosing appropriateness
Alarm burden	Alarms per operating hour, classified by cause	Guiding training and improving operation

Audit and Improvement

The improvement cycle begins by establishing definitions and denominators, then measuring a baseline, selecting a modifiable problem, implementing a specific intervention, and repeating the measurement. For example, if filter life is short, the reasons each circuit ended are reviewed rather than changing anticoagulation for all patients. Planned replacement, transport, and recovery must be distinguished from clotting when analyzing filter life. [20]

Balancing measures are also monitored: an intervention may improve filter life but increase bleeding, laboratory testing, or workload. Improved dose delivery or fewer alarms also do not demonstrate improved mortality; interpretation of clinical outcomes requires consideration of illness severity and changes in patient characteristics and the severity of their conditions. Audit is used to guide education and improve care processes, with serious events reviewed individually. [2, 20]

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The End