Complications associated with Continuous Kidney Replacement Therapy

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Disclosures: S. Gautam reports the following: Ownership Interest: Stockholder in Invitae, Sensonics, Criper, BNGO and Pacific Biosciences. B. Jaar reports the following: Honoraria: American Board of Internal Medicine - Nephrology; Patents or Royalties: UpToDate; and Advisory or Leadership Role: Clinical Journal of the American Society of Nephrology; American Board of Internal Medicine; National Kidney Foundation; BMC Nephrology; BMC Medicine. J. Lim has nothing to disclose.

Funding: None

Author Contributions: Samir Gautam: Conceptualization; Writing - original draft; Writing - review and editing Jonathan Lim: Writing - original draft Bernard Jaar: Conceptualization; Supervision; Writing - review and editing

Data Sharing Statement:

Clinical Trials Registration:

Registration Number:

Registration Date:

The information on this cover page is based on the most recent submission data from the authors. It may vary from the final published article. Any fields remaining blank are not applicable for this manuscript.
Complications associated with Continuous Kidney Replacement Therapy

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Abstract

Continuous kidney replacement therapy (CKRT) is a form of renal replacement therapy which is used in modern intensive care units (ICUs) to help manage acute kidney injury (AKI), end-stage kidney disease (ESKD), poisonings and some electrolyte disorders. CKRT has transformed ICU care of patients over the past several decades. In this setting, it is important to recognize CKRT associated complications but also up to date management of these complications. Some of these complications are minor, but others may be more important, even life threatening. CKRT related complications may be related to dialysis factors and others to specific patient factors. Our overarching goal in this manuscript is to review and discuss the most significant CKRT related complications at different steps of management of CKRT. With the advent of newer solutions there has been newer complications as well.
Introduction

Continuous kidney replacement therapy (CKRT) is a form of renal replacement therapy which is used in modern intensive care units (ICUs) to help manage acute kidney injury (AKI), end-stage kidney disease (ESKD), poisonings and some electrolyte disorders. CKRT has transformed ICU care of patients over the past several decades. As has been well-documented in prior studies, AKI incidence has been increasing, in large part driven by an older population with more comorbidities\(^1\)\(^2\). The delivery of care using CKRT has also evolved over the years, its indications has broadened, and it is being increasingly used. In this setting, it is important to recognize CKRT associated complications but also up to date management of these complications. Some of these complications are minor, but others may be more important, even life threatening. CKRT related complications may be related to dialysis factors and others to specific patient factors. Our overarching goal in this manuscript is to review and discuss the most significant CKRT related complications at different steps of management of CKRT (Fig. 1 and 2).

In the following content, we will describe and discuss management of clinically relevant CKRT complications separated by those related to vascular access, extracorporeal system and biomembranes, metabolic and electrolytes, and those related to clearance and anticoagulation (Figure 5).
**Vascular Access complications**

Vascular access are the lifeline of CKRT. Vascular access complications can arise during placement or during maintenance whether it is in the acute setting or chronic settings, each of them have their own unique limitations and complications.

During placement the common complications similar to all central vascular access line placements are arterial puncture, venous rupture, leading to bleeding, and in addition for the chest line procedures, pneumothorax, myocardial rupture and arrhythmias.

While these are complications at the time of catheter placement, the catheters can have further complications based on timing of the catheter placement which can be infectious or non-infectious (Fig 3). Non-infectious complications can be within the duration of CKRT or can persist over a number of years like central venous stenosis or even difficulty with catheter extraction. The non-tunneled catheters have limitations with possible increased risk of infections and also mechanical complications with comparisons discussed in the section below.

However, with the clinical practice guideline recommendations of using ultrasound guided techniques for placement of vascular access, the initial complications have been minimized\(^3\), \(^4\). Catheter related thrombosis is another dreaded complication and the patients on CKRT are at increased risk given concurrent illness and hypercoagulable state. If found, systemic anticoagulation is indicated as long as the catheter remains in place\(^5\).

**Nosocomial complications**

Most common vascular access complications are similar to catheter access issues seen during intermittent hemodialysis. Infectious complications of vascular accesses are one of the impediments of caring for patients in intensive care units. The infectious process typically starts from the spectrum of skin colonization, biofilm development, local exit site infection, tunnel infection and to bacteremia; however, bacteremia may also be acquired intraluminary.
Organisms are generally staphylococcus aureus, coagulase negative staphylococcus but gram-negative bacteria and candida are other possible causes of sepsis. Multiple observational studies and guidelines recommend avoiding femoral catheter sites because of an increased risk of nosocomial infections; however, in a concealed, randomized, multicenter, evaluator-blinded, parallel-group trial of 750 patients of 9 tertiary care centers, no clinically relevant benefit of jugular site catheterization was found compared with femoral site catheterization in terms of nosocomial complication in critically ill adults requiring renal replacement therapy. Jugular catheters had a statistically significantly higher rate of hematoma formation compared to the femoral group (3.6% vs 1.1%; p=0.03) but no difference in arterial puncture. In regard to catheter related infections and catheter colonization at time of catheter removal, there was no statistically significant difference between infection in the jugular and femoral catheter groups. Further, in subgroups analysis, the researchers found a statistically significant higher rate of catheter colonization at time of catheter removal with femoral catheters in patients in the highest tercile of BMI (>28.4 kg/m²). Jugular catheters had statistically significantly more gram-positive bacteria (P=0.04) and femoral catheters had a higher colonization of gram-negative bacteria (P=0.03). Duration of catheter did not seem to have a statistically significant change in catheter colonization at time of removal when the two groups compared were ≤ 5 days and >5 days.

The 2019 KDOQI guidelines recommend to limit use of temporary, noncuffed, non tunneled dialysis catheter to 2 weeks due to increased risk of infections in patients that need emergent vascular access which certainly has to be reviewed based on patient-to-patient basis as described below. There are variations to this practice too based on the patient's needs, ability to maintain CKRT patency and minimize treatment or dialysis interruption. This is a change from previous guideline recommendations that noncuffed, nontunneled dialysis catheter not exceed 3 weeks for
jugular and 5 days for femoral access\textsuperscript{8, 9}. In a retrospective study of 595 patients receiving CKRT, looking at rates of adverse events, other catheter related complications included bleeding (23\%), arterial puncture (1\%), hematoma (2.85\%), line-related infection (5\%), and other (11.93\%, pneumothorax, catheter misplacement and air embolism)\textsuperscript{10}. While non-tunneled dialysis catheter placement has been standard and common, a 16-month period observational prospective cohort study involving 154 patients, showed that compared with non-tunneled dialysis catheters, tunneled dialysis catheters were associated with better dialysis delivery and fewer mechanical complications. Interestingly, there was no difference in the rate of positive blood cultures per catheter \textsuperscript{11}. Further randomized studies will need to confirm these findings.

**Extracorporeal Circuit Complications**

*AN69 and ACE Inhibitor:* AN69 is polyacrylonitrile synthetic dialysis membrane which was developed to improve biocompatibility. AN69 membranes have been associated with anaphylactoid reactions when used in combination with ACE inhibitors due to activation of bradykinin. These reactions have been partially mitigated by surface treatment of the AN69 membrane (AN-69ST)\textsuperscript{12}.

*Hypothermia*

One of the most noted significant adverse events of CKRT is hypothermia, defined as a temperature $<35^\circ\text{C}$, and was found in up to 44\% of patients in one study\textsuperscript{10}. Under 34 $^\circ\text{C}$, hypothermia can cause depressed brain and cardiovascular function, arrhythmia, mask fevers delaying recognition of infections and initiations of antibiotics\textsuperscript{13}. Critically ill patients on CRRT are predisposed to hypothermia from many factors including, but not limited to, sedation,
paralytics, shock, endocrine disorders, intoxications and CNS lesion/injury. Of note, arterial and venous line temperatures differences during CKRT have been studied. The largest temperature difference between blood in arterial and venous lines was 5.5 °C +/- 0.2 °C when blood flow (Qb) was 100 mL/minute and dialysate flow (Qd) was 1,500 mL/hour. The lowest temperature difference was 1.9 °C +/- 0.1 °C when Qb was 200 mL/min and Qd was 500 mL/hr, showing that slower Qb and higher Qd caused greater energy lost during CKRT14. In another study, heat loss was calculated to average 750 kcal/day, worsening caloric deficit in these already critically ill patients. However, in some situation, cooling may be beneficial such as in patients with significant hyperthermia and status post cardiac arrest13. Milder degrees of hypothermia may contribute to more hemodynamic stability by causing an increase in pulse, cardiac output and systemic vascular resistance. In a prospective crossover randomized study, 30 patients on continuous veno-venous hemofiltration (CVVH) had a heating device set to 38 °C and 36 °C for 6 hours each. The authors found that patients core temperature didn’t change significantly; however, patients with CVVH with a heating device set at 36 °C had higher mean arterial pressure and required lower catecholamine infusion doses15.

Suggestions for treatment of hypothermia include passive external rewarming (blankets allow for natural thermogenesis to raise core temperature by 0.5 °C/h if shivering mechanism is intact). But also active external rewarming (warming devices are reported to raise temperature by 1 to 2.5 °C/hour) and active internal/core rewarming (IV fluids warmed up to 42 °C, peritoneal dialysate, isotonic crystalloids into stomach or bladder). Of note, modern dialysis machines are equipped with warming devices to help counter heat loss as well13.

*Citrate toxicity*
Because of the nature the extracorporeal circuit, contact of blood with the biomembranes, and procoagulant state, critically ill patients on CKRT frequently require anticoagulation to prolong the life of the filter and to minimize interruptions of the dialysis therapy\textsuperscript{16}. The most common anticoagulants used during CKRT are intravenous heparin or regional citrate anticoagulation (RCA)\textsuperscript{17}. The RICH study showed that the patients with intravenous heparin had higher rate of bleeding compared to regional citrate but regional citrate had higher rate of culture proven infection compared to intravenous heparin\textsuperscript{18}. In addition, it is also important to recognize associated metabolic complications (Hypocalcemia and hypercalemia, hypernatremia, metabolic alkalosis) and also citrate toxicity (Fig 4)\textsuperscript{19}. However, it's important to note that a recent post hoc analysis of the RICH trial revealed that longer mean filter lifespan (>48 hours) was associated with an increased rate of new infections, independent of the type of anticoagulation used\textsuperscript{20}.

Citrate toxicity can be identified by a low ionized calcium, a disproportional rise in total calcium with a total calcium/ionized calcium ratio of >2.5 and high anion gap metabolic acidosis or with escalating rates of calcium infusion\textsuperscript{19}. Citrate excess has also been associated with metabolic alkalosis which occurs when citrate is metabolized to bicarbonate in the liver\textsuperscript{21}. These complications can be managed by decreasing the citrate rate or increasing the dialysis or effluent rate, all of which would be geared towards decreasing citrate delivery\textsuperscript{22}. Importantly, RCA is best avoided in patients who have acute liver failure, cardiogenic shock with high lactate levels (>8mmbol/L) as they have a high risk of impaired citrate metabolism, with high risk of citrate accumulation and citrate toxicity. For other rare instances of citrate dynamics, it is important to recognize there can be three potential scenarios which can cause different acid base and electrolyte disorders. Citrate accumulation can cause metabolic acidosis due to delayed metabolism of citrate and leading to lactic acidosis. This can be fatal but given intensive
monitoring it is of rare occurrence. Increased citrate infusion can lead to metabolic alkalosis and hypernatremia\textsuperscript{23, 24}.

The manifestations of citrate overload depend on the metabolic state, rate of citrate infusion or type of citrate used. Citrate chelates with calcium and it has to be used as proximal as possible to the access to reduced the initiation of coagulation cascade. The citrate binds with calcium to creatinine Calcium Citrate Complex (CCC) most of which would be cleared with CKRT\textsuperscript{21, 24}. But as if escapes to the systemic, citrate gets metabolized to bicarbonate and also releases sodium, thus metabolic alkalosis and hypernatremia can occur. Severity of hypernatremia depends on the type of citrate used like TCA which has 420 mmol/L of sodium compared to ACD 224 mmol/L of sodium\textsuperscript{24}.

**Hematologic complications**

Hematologic complications are one of the most underrecognized complications observed in patients during CKRT. These complications could be related to anticoagulation (heparin, citrate) or as a result of extracorporeal circuit related issues. The most common complication is thrombocytopenia but anemia have also been reported.

*Thrombocytopenia*

CKRT may be associated with thrombocytopenia and can confound the diagnosis and management of other causes of thrombocytopenia seen in critically ill patients such as sepsis, heparin-induced thrombocytopenia, and drug-related thrombocytopenia\textsuperscript{25}. The temporal relationship of CKRT and decrease in platelet count with CRRT initiation and follow-up was evaluated at a quaternary regional referral center where 80 patients who received CRRT for
greater than 48 hours and were followed for thrombocytopenia (defined by a platelet count of less than 100k/uL) with a platelet count stable for at least 4 days before CKRT initiation. During a five-day course, there was significant worsening thrombocytopenia in 59.1% of patients at day 5, including 29.5% of patients who developed even more severe thrombocytopenia of less than 50,000/uL. In this study, only Sequential Organ Failure Assessment (SOFA) score at time of CKRT initiation on multivariate analysis predicted the development of thrombocytopenia. In regards to heparin-induced thrombocytopenia (HIT), of the 20% of patients suspected and evaluated, 81.2% had a low to intermediate pre-test probability of HIT but only 1 patient had laboratory confirmed HIT26.

The mechanism of thrombocytopenia in CKRT is unclear, and likely multifactorial as critically ill patients on CKRT have many comorbidities that can be associated with thrombocytopenia. Platelet destruction, adsorption, and activation are likely to play a role. In one study, Indium-labelled platelets in an invitro system showed considerable platelet deposition on a variety of dialysis membranes27, 28. Seen in other extracorporeal membranes, platelet activation was postulated to have a role in thrombocytopenia in CKRT through peripheral consumption. However, evidence for platelet activation has been mixed27, 29. Thrombocytopenia may also have prognosis values at the time of CKRT initiation. In a recent study by Griffin et al., the authors reported that a more than 40% decreased in platelet count was associated with increased risk of secondary infections. Interestingly, the same research group reported that thrombocytopenia was associated with lower rates of renal recovery and higher mortality28, 30, 31.

Management is variable and could consist of higher blood flows which is postulated to decrease transit time, improved rheology and decreased hemoconcentration28. Transition to intermittent hemodialysis is postulated to decrease contact time with dialysis filter. However, not many
studies have evaluated thrombocytopenia across different renal replacement therapy (RRT) modalities. In one study, CKRT was associated with a platelet decrease compared to intermittent hemodialysis but only in univariate analysis. Nonetheless, the results were attenuated when accounting for severity of illness, liver disease, filter losses. In the same study, the intermittent hemodialysis group had twice as much filter exposure compared to the conventional group, and more thrombocytopenia but this was not statistically significant$^{28,32}$.

Anemia

Anemia may occur in patients on CKRT for a variety of reasons. In a retrospective study assessing adverse events in adults on CKRT, one study found 31% of the 595 patients to have new onset anemia defined as a hemoglobin $<10$ g/dL. One leading cause of anemia is blood lost through extracorporeal circuit. In a subgroup analysis comparing blood loss of CKRT to intermittent hemodialysis, it shows that patients with CKRT had increased RRT related blood loss but the transfusion events were similar$^{33}$. The clotting cascade is activated with shearing and turbulence induced by non-endothelialized surface of the filter, circuit tubing and catheter. RCA has extensively been evaluated. A meta-analysis of 11 randomized controlled trials (RCTs) of approximately 2000 filters and 1000 patients demonstrated RCA for CKRT was able to reduce risk of extracorporeal circuit blood loss compared to regional and systemic heparin administration and is the recommended anticoagulant in the most recent KDIGO guidelines if there are no contraindications$^{4,34}$. Compared to systemic heparin administration, circuit lost (circuit termination for any reason) was significantly reduced by 24% with RCA. On the other hand, compared with regional heparin anticoagulation, circuit lost had a 48% significant reduction with RCA. Information regarding filter failure (filter clotting or high transmembrane filter pressure) was available in 6 RCTs, and found in the pool data to favor the citrate group
with the important caveat of high inter-trial heterogeneity. Catheter dysfunction was similar between both groups. In the 9 trials that compared systemic heparin to RCA, the bleeding risk was significantly reduced with RCA. 35.

Another reason for the anemia observed during CKRT, is mechanical hemolysis from the extracorporeal circuit itself. More commonly seen in extracorporeal membrane oxygenator circuits (ECMO), small studies looking into plasma free hemoglobin (PFHb) from CKRT circuits showed statistically significant rise in PFHb but not to the levels of clinically significant hemolysis reported in the ECMO literature. Whereas, filter clotting and peak circuit pressures did not have any statistically significant change in PFHb in another small study32.

**Electrolyte Disturbances**

*Hypophosphatemia*

Like many of the adverse events seen in critically ill patient receiving acute dialysis, the etiology of hypophosphatemia is multifactorial as well34. It is important to note that hypophosphatemia is typically an avoidable complication. Malnourishment, re-feeding syndrome, sepsis, insulin and phosphorous removal during CKRT, all contribute to hypophosphatemia in this critically ill population. Some studies that looked at effectiveness of established phosphate repletion protocols still resulted in patients developing hypophosphatemia23, 36. Even though there isn’t evidence that intensive CRRT dose improve survival rate of critically ill patients with AKI, there are instances where intensive CRRT is needed like acute hyperammonemia or severe, labile hyperkalemia37, 38. However, this intensive treatment may increase the risk of developing hypophosphatemia39. Further, there isn’t a consensus agreement about phosphate goal during
CKRT, but there is evidence that hypophosphatemia at all ranges is associated with worse outcomes\textsuperscript{23}. Hypophosphatemia <0.6 mmol/L (1.86 mg/dL) have been reported to increase the incidence and duration of mechanical ventilation\textsuperscript{38}. Similarly, hypophosphatemia <0.67 mmol/L (2 mg/dL) has been associated with increased need for tracheostomy\textsuperscript{40}.

Some have advocated for phosphate containing dialysate as a different approach to prevent CKRT induced hypophosphatemia. Commercially available dialysate replacement fluid containing phosphate at 1.2 mmol/L has been studied and indeed helped maintain normophosphatemia in the majority of patients\textsuperscript{23, 41}. However, rare cases of hyperphosphatemia, metabolic acidosis and hypocalcemia have been reported. Currently, there is no consensus about the optimal phosphorous target in CRRT patients and importantly, there are concerns about serum levels not being reflective of intracellular phosphorous concentrations and subsequent ATP synthesis\textsuperscript{38}. So further studies are needed to evaluate adequate phosphorus targets to avoid complications associated with CRRT induced hypophosphatemia\textsuperscript{38, 40}. Of note, phosphate containing solutions come with 0 glucose and recently, there have been reports of patients developing normoglycemic ketoacidosis. This phenomenon is increasingly recognized in patients who are using glucose free CKRT solutions and sometimes even with glucose containing CKRT solutions. Normoglycemic ketoacidosis is identified with anion gap metabolic acidosis, serum ketones and low/normal glucose. The treatment of this phenomenon involves infusion of glucose and insulin\textsuperscript{42, 43}.

In addition to calcium, we also need to monitor magnesium levels, while the patient is using regional citrate anticoagulation as the citrate also chelates magnesium and patient becomes systematically depleted with magnesium levels\textsuperscript{44}.

In addition to phosphorus, importantly there is a need to monitor other electrolyte imbalances such as potassium, calcium and sodium. While potassium and calcium disorders can be mitigated by changing the dialysate or replacement fluid electrolyte mixture, sodium disorders will require additional management. Severe AKI and hyponatremia with risk of overcorrection can be
managed by adding hypotonic fluids through the circuit or adjusting the CKRT solutions\textsuperscript{45}. Customizing CKRT solutions by adjusting the sodium concentrations in the solution is possible with the multidisciplinary effort by pharmacists according to the sodium levels\textsuperscript{46}. Sodium follows urea kinetics and using this model, it is possible to predict the change in sodium levels by making changes in the CKRT solution\textsuperscript{47}. Similarly, circumstances which require hypernatremia, like acute neurologic injuries such as intracranial hemorrhage, stroke will also require custom CKRT solutions or hypotonic fluids.

\textbf{Treatment delivery and Volume management}

Although there is no proven lower threshold of CKRT dose in AKI, the KDIGO guidelines recommend to aim for delivered effluent of 20-25 mL/kg/hr for CKRT in this setting; however, because of downtime due to different reasons such as imaging studies, CRRT breakdown, need for surgeries, patients don’t always get the desired dose\textsuperscript{48, 49}. Venkatraman et al. showed that patients who were prescribed 24 mL/kg/hr, in fact received 16 mL/kg/hr with RRT running for 16 hours (67\%) on average\textsuperscript{50}. Therefore, to ensure a minimum delivered dose of 20–25 mL/kg/hr, it may be necessary to prescribe approximately 25–30 mL/kg/hr, and it is also necessary to minimize CKRT downtime to 4 h per day or less\textsuperscript{48-50}.

Cardiac stunning

In addition to clearance, more recently we have had a better understanding of the impact of ultrafiltration rates on patient survival. Too aggressive ultrafiltration can cause hypotension and myocardial stunning. In hemodialysis patients, this has shown to increase the risks of sudden cardiac arrests. In critically ill patients also, initiation of CKRT has been associated with cardiac
Cardiac stunning is not only related in patients with aggressive ultrafiltration but also in patients without aggressive ultrafiltration and these patients have extremely high mortality\textsuperscript{52}.

Dialysis disequilibrium syndrome:

Dialysis disequilibrium syndrome (DDS) is one of the complications that can occur after initiating the patients on renal replacement therapies due to rapid shifts of solutes. Although, CKRT has been postulated to have slower clearance of solutes thereby decreasing the risks of DDS, however, there have been few case reports that DDS has occurred in patients receiving CKRT\textsuperscript{53}. There needs to be educations on overriding the alarms, careful adjustments of electrolyte mixtures to prevent further electrolyte derangements especially with commercially available solutions.

**Metabolic support/Nutritional losses**

Patients in ICU are typically in a catabolic state and require high intake of amino acids and micronutrients. In addition, most of these patients are hypoalbuminemic due to their critical illness but also as a consequence of their CKRT treatment. In addition to providing clearance for solute and ultrafiltration, the CKRT membranes also clear micronutrients and macronutrients. Consequently, patients on CKRT lose water soluble amino acids. Nutritional losses represent a significant concern for patients on kidney replacement therapies. Careful administration of calories and nutrients in close coordination with the nutritionist would be desirable and while switching the modalities, the changing clearance of amino acids and micronutrients needs to be considered. KDIGO guidelines recommend protein intake up to 1.7 g/kg/day in patients on
We also need to adjust the addition to calories with citrate or lactate as they also provide extra calories.

**Deconditioning**

One of the barriers of patients receiving CKRT is delayed mobility due to being connected to the machines in addition to their critical illness and often endotracheal intubation with mechanical ventilation. However, physical therapy in the ICU has been reported to improve outcomes and even physical functioning. Specifically in the setting of ongoing CKRT treatment, more recently there have been reports showing good safety profile and feasibility of physical therapy. In addition, when possible, the use of hybrid kidney replacement therapies may allow for early mobilization. As a reminder, any attempts of early weaning off CKRT, should be on the checklist of ICU rounding.

**Drug delivery and clearance**

Generally, for patients on intermittent renal replacement therapies the drug dosing is for a GFR of < 10 mL/minute/1.73m²; however, there is risk of inappropriate drug clearance with continuous renal replacement therapy or prolonged intermittent renal replacement therapy, especially, antibiotics in septic patients resulting in under dosing of antibiotics or any other medications. This is important especially if you are treating a patient with septic shock or status epilepticus. There is paucity of data on individual clearance of medications by CKRT and there is different degree of clearance on individual drugs based on the modality and dose of CKRT, volume of distribution, sieving coefficient, and protein binding of the drugs. In addition, to this the medication dosing can be estimated by multiplying the effluent with (1-protein binding) and also need to adjust for prefilter dilution.
Conclusion

CKRT plays a very important role in the modern ICU and we need to be mindful about the common complications observed with this renal replacement modality and also how to mitigate some more difficult to avoid complications associated with CKRT. Often, the patients have a septic profile with increasing comorbidities. There needs to be more vigilance in nutritional support and volume management. While the CKRT has been around for a few decades, there is a need to utilize safety and quality mechanisms to standardize the care, undergo root cause analysis and collaborate with different types of ICUs. Ultimately, excellent coordination with multidisciplinary teams including nurses, pharmacists, nutritionists, intensivists is key to the success of CKRT in the modern ICU setting.

Disclosures:

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Funding

None.

Acknowledgments
The content of this article reflects the personal experience and views of the author(s) and should not be considered medical advice or recommendation. The content does not reflect the views or opinions of the American Society of Nephrology (ASN) or Kidney360. Responsibility for the information and views expressed herein lies entirely with the author(s).

Authors contributions

Bernard Jaar: Conceptualization; Supervision; Writing - review and editing. Jonathan Lim: Writing - original draft. Samir Gautam: Conceptualization; Writing - original draft; Writing - review and editing.

References


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Figure 1: CKRT Cycle and Complications

Figure 2: Complications Associated with CKRT

Figure 3: Complications of catheter placement

Figure 4: Complications of regional citrate anticoagulation

Figure 5: Complications Associated with Continuous Kidney Replacement Therapy
CKRT INITIATION AND OUTLINE OF GOALS OF THERAPY

Vascular access - Insertion complications

Air embolism and bleeding during catheter removal
Vascular access late complications

Electrolyte disturbances
Hematologic complications
Nutritional deficiencies
Vascular access complications
Normoglycemic Ketoacidosis
Cardiac stunning
Deconditioning
Drug clearance

WEANING

MAINTENANCE

Figure 1: CKRT cycle and complications
Figure 2: Complications Associated with CKRT

- Hematological complications
- Vascular access and patency maintenance complications
- Electrolytes and acid base disorders
  - Normoglycemic ketoacidosis
- Drug clearance
- Hypothermia
- Volume related
- Cardiac stunning
- Nutritional
  - Physical Deconditioning
Figure 3: complications of catheter placement

Catheter placement
- Injury to vessel wall
- Thrombus
- Air embolism
- Bleeding
- Arterial puncture

Infectious
- CLABSI
- Diskitis, septic arthritis, spinal epidural abscess

Non-Infectious
- Early < 1 week
- Hematoma
- Pneumothorax
- Pericardial tamponade
- Arrhythmia
- Air embolism
- Bleeding
- Arterial puncture

Non-Infectious
- Late
- Exit site infection - within < 2 cm
- Tunnel infection - >2 cm
- CLABSI
- Complications of CLABSI - endocarditis, discitis, septic arthritis, spinal epidural abscess
Figure 4: Complications of regional citrate anticoagulation

- Human error
  - Failure to stop citrate infusion when machine not in use

- Citrate toxicity

- Regional Citrate anticoagulation

- Citrate metabolic effects (added calories, lactic acidosis)

- Hypernatremia
- Hypocalcemia
- Metabolic acidosis
- Metabolic alkalosis
- Hypomagnesemia
<table>
<thead>
<tr>
<th>Factors</th>
<th>Potential Complications</th>
<th>Prevention</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Access</td>
<td>• Bleeding</td>
<td>• Assess for coagulopathy</td>
<td>• Reverse coagulopathy prior to procedure</td>
</tr>
<tr>
<td></td>
<td>• Insertion:</td>
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<tr>
<td></td>
<td>o Thrombosis</td>
<td>• Use of ultrasound guided vascular access placement</td>
<td>• Reverse Trendelenburg position as indicated</td>
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<tr>
<td></td>
<td>o Hematoma</td>
<td>• Confirm catheter position before use</td>
<td>• Chest tube placement as indicated</td>
</tr>
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<td></td>
<td>o Pneumothorax</td>
<td>• Monitoring of peak and plateau pressures</td>
<td></td>
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<td></td>
<td>o Pericardial tamponade</td>
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<td>o Arrhythmia</td>
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<td>• Making sure the placement of tip at SVC and right atrium junction</td>
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<td>• No role for prophylactic anticoagulation to prevent catheter dysfunction.</td>
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<td></td>
<td>• Catheter manipulation, patient positioning, use of rTPA*** for early non infectious complications</td>
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<td>Extracorporeal Circuit</td>
<td>Infection (catheter exit site / sepsis)</td>
<td>Aseptic technique</td>
<td>use of topical antibiotics</td>
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<td>• Catheter care</td>
<td>• Remove catheter as soon as possible</td>
</tr>
<tr>
<td></td>
<td>• Higher risk when CRRT* is connected to other extracorporeal circuits</td>
<td></td>
<td>• Cultures / antibiotics as appropriate</td>
</tr>
<tr>
<td></td>
<td>• Need to connect before oxygenator in ECMO**</td>
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<tr>
<td>Extracorporeal Circuit</td>
<td>Air embolism</td>
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<tr>
<td></td>
<td>• Make sure the venous arm is clamped first</td>
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<tr>
<td></td>
<td>• Oxygen support</td>
<td></td>
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<tr>
<td></td>
<td>• Positioning the patient as if it is a systemic air embolism or pulmonary air embolism</td>
<td></td>
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<tr>
<td>Reduced filter life</td>
<td>• Reviewing and educating the CRRT pressure settings</td>
<td></td>
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<tr>
<td>Reduced filter life</td>
<td>• Implementing the protocols based on institution comfort and needs</td>
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<tr>
<td>Reduced Dialysis dose</td>
<td>• Adjusting the CRRT solutions and blood flow rates</td>
<td></td>
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</tr>
<tr>
<td>Reduced Dialysis dose</td>
<td>• Anticoagulation protocols based on patient needs</td>
<td></td>
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</tr>
<tr>
<td>Reduced Dialysis dose</td>
<td>• Proactive reviewing the CRRT pressure readings</td>
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<tr>
<td></td>
<td>Monitoring</td>
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</tr>
<tr>
<td></td>
<td>Hypothermia</td>
<td>Use other methods of detecting sepsis</td>
<td>Using CRRT warmer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Newer CRRT machines allows to adjust temperature</td>
<td>Sometimes therapeutic for patients with hyperthermia</td>
</tr>
<tr>
<td></td>
<td>Hematologic</td>
<td></td>
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<tr>
<td></td>
<td>Anticoagulation</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>a. Citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i. Hypocalcemia</td>
<td>Risk stratification of patients for clotting versus bleeding</td>
<td>Prefilter or post filter saline for metabolic alkalosis and at times to compensate for respiratory alkalosis</td>
</tr>
<tr>
<td></td>
<td>ii. Metabolic alkalosis</td>
<td>Monitor for citrate adequacy and citrate toxicity with ionized to total calcium ratio, excessive need for calcium infusion</td>
<td>Adjust the citrate dose and or change the rates of calcium infusion and CKRT solutions rate based on hypocalcemia or evidence of citrate toxicity/accumulation</td>
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<tr>
<td></td>
<td>iii. Hypernatremia</td>
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<tr>
<td></td>
<td>iv. Citrate intoxication</td>
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<td></td>
<td>v. Bleeding-rare</td>
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<td></td>
<td>b. Heparin and other anticoagulation</td>
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<tr>
<td></td>
<td>i. Heparin-induced thrombocytopenia</td>
<td>Close monitoring of platelets and hemoglobin</td>
<td>Adjust heparin dose</td>
</tr>
<tr>
<td></td>
<td>ii. Bleeding</td>
<td>Monitoring of coagulation panel</td>
<td>Use alternatives like Bivaluridin, Argatoban according to patient needs</td>
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<tr>
<td></td>
<td>2. Bleeding</td>
<td>Sudden loss of circuit</td>
<td>Proactive changing of filters</td>
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<td></td>
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<td></td>
<td>Educating and monitoring the access pressures</td>
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<tr>
<td>Electrolytes and acid base</td>
<td>Hemolysis</td>
<td>Physical Deconditioning</td>
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<tr>
<td>• Hypophosphatemia</td>
<td>• Especially in patients with integrated circuits, watch LDH, haptoglobin</td>
<td>• Frequent weaning trials</td>
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</tr>
<tr>
<td>• Hypomagnesemia</td>
<td>• Reassess the continuation of CRRT, changing the flow rates</td>
<td>• Physical therapy</td>
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<tr>
<td>• Hypocalcemia</td>
<td>• Daily basic metabolic profile or more frequently as needed</td>
<td></td>
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<tr>
<td>• Hypokalemia</td>
<td>• Monitor anion gap closely and check beta hydroxybutyrate level</td>
<td></td>
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<tr>
<td>• Hyponatremia</td>
<td>• Adjustment of dialysate or replacement fluids electrolytes or flow rates</td>
<td></td>
<td></td>
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<tr>
<td>• Hypernatremia</td>
<td>• Replete electrolytes</td>
<td></td>
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<tr>
<td>• Normoglycemic Ketoacidosis</td>
<td>• Insulin and glucose drip</td>
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</tr>
</tbody>
</table>

**Electrolytes and acid base**

- Hypophosphatemia
- Hypomagnesemia
- Hypocalcemia
- Hypokalemia
- Hyponatremia
- Hypernatremia
- Normoglycemic Ketoacidosis

**Nutritional losses**

- Amino acids and proteins
- Poor glycemic control
- Vitamin deficiencies
- Trace minerals

**Physical Deconditioning**

- Frequent weaning trials

*CCRT: Continuous renal replacement therapy; **ECMO: Extracorporeal membrane oxygenation, ***rTPA: Recombinant tissue plasminogen activator*