Continuous Renal Replacement Therapy: Reviewing Current Best Practice to Provide High-Quality Extracorporeal Therapy to Critically Ill Patients

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Continuous renal replacement therapy (CRRT) use continues to expand globally. Despite improving technology, CRRT remains a complex intervention. Delivery of high-quality CRRT requires close collaboration of a multidisciplinary team including members of the critical care medicine, nephrology, nursing, pharmacy, and nutrition support teams. While significant gaps in medical evidence regarding CRRT persist, the growing evidence base supports evolving best practice and consensus to define high-quality CRRT. Unfortunately, there is wide variability in CRRT operating characteristics and limited uptake of these best practices. This article will briefly review the current best practice on important aspects of CRRT delivery including CRRT dose, anticoagulation, dialysis vascular access, fluid management, and drug dosing in CRRT.

Key Words: CRRT, CRRT dose, Critical illness, Anticoagulation, Timing of dialysis

INTRODUCTION

Continuous renal replacement therapy (CRRT) has been evolving briskly over the last 40 years.[1] While in some circles, there remains a robust debate on the merits and role of CRRT compared to other methods of renal replacement therapy (RRT) such as intermittent hemodialysis (IHD), prolonged intermittent RRT, and peritoneal dialysis, for many reasons, CRRT has become the dominant modality of acute RRT in critically ill patients in resource-rich areas throughout Europe, North America, Asia, and Australia.

This article will not wade into these important issues or questions regarding modality of acute RRT, but rather will attempt to summarize best practice in the delivery and application of CRRT. While many readers will have strong opinions on whether CRRT provides more benefit than struggle, hopefully, we can all agree that when CRRT is prescribed, it is our duty to optimize and target therapy to achieve the desired goals by using the best available evidence and guidelines.

DEFINING HIGH-QUALITY CONTINUOUS RENAL REPLACEMENT THERAPY

Many countries define quality metrics for chronic IHD for end-stage kidney disease patients, yet, in the United States at a minimum, there are no current reportable quality metrics for acute RRT or CRRT. As a result, there has been little unified or systematic effort to improve CRRT quality in the United States yielding a striking variability in practice patterns between both experienced centers and providers.

Providing high-quality CRRT is a complex endeavor that involves a multidisciplinary team with a unified vision. For example, clinician experts must consider mode of clearance (convective, diffusive, or both), small solute clearance rate, fluid removal targets, CRRT circuit anticoagulation strategies, and vascular access to name a few. Nurses deliver CRRT therapy making sure to setup and maintain the machine with the prescribed operating characteristics (using the proper solutions, etc.) while attempting to meet fluid removal targets and troubleshoot vascular access and the CRRT circuit to decrease CRRT circuit failures. Nutrition and pharmacy support colleagues need to adjust medication dosing and nutrition support needs.

Failures anywhere along this complex tree lead to suboptimal CRRT, failure to achieve the individualized goals of therapy, and can negatively impact patient outcomes. While critical care medicine specialists are increasingly experienced with CRRT, we endorse that there remains a broad role for collaborating nephrologists to assist in the management of acute kidney injury (AKI) and acute RRT in the critically ill patient.[2] Highlighting the multidisciplinary nature of CRRT, Table 1 describes a six-step framework for delivering high-quality CRRT, and facilitating high-quality CRRT with a tailored precision medicine approach was the subject of the 17th Acute Dialysis Quality Initiate (ADQI) International Consensus Conference.[1]

Given the complexity of CRRT, it is impossible to employ a single metric to define and benchmark high-quality, precision CRRT or monitor a programs performance. Table 2 outlines possible metrics and benchmarks that could be used in CRRT.

Hard end points such as survival, and kidney function recovery (in AKI) to liberation from RRT are more difficult to benchmark because multiple patient factors competitively influence these outcomes in the intensive care unit (ICU) and there are large differences in expected mortality rates based on the type of patient and severity of illness (both of which differ between various subspecialized ICUs and hospitals). Precision CRRT certainly requires attention to both CRRT modality and total effluent flow rate targets ("CRRT dose") when prescribing therapy. Yet, there is ample data that support a gap between prescribed and achieved/delivered CRRT dose,[3,4] suggesting

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that a benchmark of prescribed dose alone is an inadequate metric. While fluid overload is now clearly recognized as contributing to poor outcomes in ICU patients,[5-11] fluid balance targets must be individualized for each patient based both on disease process and stage of illness thus making it difficult to benchmark across different ICUs or institutions.

Despite the challenges of benchmarking, clinicians should be encouraged that there is an expanding evidence base to inform best practice and consensus statements which should guide decision making for individual patients while also fostering for programmatic quality assurance (QA) and improvement (QI) at the institutional level.

Continuous Renal Replacement Therapy Mode

Recognizing that with advancing technology came variability in nomenclature, Villa and colleagues[12] recently published an expert consensus statement to clarify CRRT nomenclature. Historically, there has long been teaching, bordering on dogma, that there is a significant difference in the middle molecule clearance between convective (hemofiltration) vs diffusive (hemodialysis) modes of clearance.[13] However, in continuous venovenous (CVV) hemofiltration (CVVH), the middle molecule clearance may be as great as 20 mL/min, while only 8-12 mL/min with CVV hemodialysis (CVVHD).[14] There is no increase in middle molecule clearance with CVV hemodiafiltration (CVVHDF), either. There remains no definitive randomized data comparing survival with continuous hemofiltration vs hemodialysis. Wide variability in practice remains around the world, and no clear consensus statements have been published on this topic.

CLINICAL SUMMARY

- High-quality continuous renal replacement therapy is a complex procedure requiring a collaborative multidisciplinary team-based approach to maximize patient outcomes.
- Use best available evidence to employ best practices in prescribing continuous kidney replacement therapy.
- Measure performance and adherence to best practices for quality assurance and quality improvement.

Certainly, purely convective modes of therapy such as CVVH will always have a higher filtration fraction (FF) compared to purely diffusive clearance as in CVVHD when blood flow, hematocrit, and total effluent flow rates are held constant.[9,15] Increasing FF should negatively correlate with CKRT circuit survival, and one small pilot data set may corroborate this trend toward fewer circuit exchanges in CVVHD vs CVVH, but this data do not reach statistical significance due to small sample size.[16] Of course, CVVHDF allows for a combination of the two modalities and whose FF lies between CVVH and CVVHD depending on the relative contribution of convection and diffusion to the total effluent flow rate. It should be noted that while using a prefilter replacement fluid strategy in CVVH or CVVHDF does decrease FF marginally, it would be naïve to assume that this alone resolves the concern of elevated FF on circuit failures and comes at the expense of decreasing small solute clearance.

At this time, the data cannot strongly support one mode of CRRT over another. We support that mode selection should be guided with the intent to maximize CRRT circuit survival and by considering planned anticoagulation practice and other factors. As will be discussed below further, standardization of certain aspects of CRRT (such as mode) can decrease variability and improve quality.

Continuous Renal Replacement Therapy Dose

Based on both the VA/NIH ATN[17] and RENAL[18] trials, clear consensus has emerged regarding CRRT dose—specifically that "high-dose" CRRT has no apparent additive benefit compared to usual dose as a standard of care. As a result, the Kidney Disease Improving Global Outcomes (KDIGO) and ADQI recommend achieving a target CRRT effluent flow rate of at least 20-25 mL/kg/h.[19,20]

However, approaching CRRT dose as a static concept is certainly not appropriate for all patients. Rather, our practice is a dynamic approach to CRRT dose focused on achieving specific daily goals but maintaining a floor of 20-25 mL/kg/h effluent flow. This individualized approach allows for a more precise approach to serve a critically ill patient's evolving needs.[15,20,21] For example, when CRRT is first initiated, severe acidemia may warrant a more aggressive CRRT dosing approach. Subsequently, CRRT effluent flow rates can (and should) be decreased to a more standard CRRT dose when homeostasis is reached to avoid the negative impacts of high-dose CRRT on nutritional status especially.

Anticoagulation

Anticoagulation of the CRRT circuit is recommended by KDIGO[19] as a strong grade 1B recommendation, and multiple studies have shown a benefit to circuit survival with a variety of different anticoagulation methods when compared to no anticoagulation.[22] The optimal anticoagulation strategy should be (1) readily available, (2) prolong filter life by preventing clotting, (3) have minimal systemic affects, and (4) have low bleeding risk. Regional citrate anticoagulation (RCA) and systemic heparin protocols are the two most widely used strategies globally. Meta-analyses and multiple additional studies support RCA as providing superior circuit survival with lower bleeding complications when compared to systemic heparin.[23-27] We believe that current best practice supports anticoagulation for CRRT circuit survival and improves the prescribed to delivered CRRT dose ratio. RCA has proven safe and effective and should be considered as a default approach. There are many published RCA protocols nicely reviewed by Morabito and colleagues[28] in 2014. It is important to note that the US FDA has yet to approve citrate use in CRRT circuits. Despite this, off-label RCA in CRRT is quickly expanding in the United States.

Certainly, RCA protocols are more complex than alternatives and require monitoring for potential adverse effects including systemic hypocalcemia, metabolic alkalosis,