Blood Purification

Precision Continuous Renal Replacement Therapy and Solute Control

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Abstract
Continuous renal replacement therapy (CRRT) remains the
dominant form of renal support among critically ill patients
worldwide. Current clinical practice on CRRT prescription
mostly relies on high quality studies suggesting no impact
of CRRT dose on critically ill patients' outcomes. Recent clin-

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ical practice guidelines have been developed based on these studies recommending a static prescribed CRRT dose of 20–25 ml/kg/h. There is a rationale for renewed attention to CRRT prescription/practice based on the concept of dynamic solute control adapted to the changing clinical needs of critically ill patients. In response, Acute Disease Quality Initiative convened a 17th consensus meeting centered on re-evaluation of CRRT. This work group developed 4 themes focused specifically on CRRT dose prescription, delivery and solute control that were summarized in a series of consensus statements, along with the identification of critical knowledge gaps. CRRT dose prescription and delivery can be based on effluent flow rate. Delivered dose should be routinely monitored to ensure coherence with prescribed dose. CRRT dose should be dynamic, in recognition of between- and within-patient variation in targeted solute control or unintended solute clearance. Quality measures specific for monitoring delivered CRRT dose have been proposed that require further validation, prior to implementation, into the practice of guiding optimal CRRT dosage.

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Introduction

Continuous renal replacement therapy (CRRT) dose delivery has conventionally been based on the clearance of urea as a surrogate for low molecular weight uremic toxins [1]. Since small solute clearance is approximately equal to CRRT effluent flow, the dose of CRRT is expressed as the effluent volume per unit of time, normalized to body weight [2]. Solute control was a key priority identified during the first Acute Disease Quality Initiative (ADQI) consensus meeting that focused exclusive on CRRT [3].

In the 16 years, since the first ADQI meeting, new evidence has emerged to address the issue of optimal CRRT dose, modality and methods for monitoring [4]. In particular, one of the recommendations for future research during the first ADQI meeting was to define a minimum dose of CRRT in the management of critically ill patients with severe acute kidney injury (AKI) [1, 5]. Two high-quality multicenter randomized trials focused on defining the association of delivered renal replacement therapy (RRT) dose and outcome in critically ill patients have been published [6, 7]. The findings of these 2 landmark trials have informed key content in recent clinical practice guidelines (CPG) for the dose prescription and delivery of CRRT in the management of AKI [4].

Greater CRRT dose has not been shown to definitively improve survival or kidney recovery among critically ill patients with AKI [5–7]. However, these findings do not preclude that CRRT dose is not important. Moreover, nearly all these clinical trials of CRRT dose evaluated only fixed dose prescriptions. It remains uncertain whether a fixed or static dose is appropriate for critically ill patients whose clinical course may change unpredictably. The concept of 'precision medicine' could conceivably be applied to CRRT care in critically ill patients. The dynamic prescription of CRRT dose in response to the clinical, physiological and metabolic needs of the patient may translate into better quality of care and improved outcomes. Moreover, dynamic CRRT prescription would provide the opportunity to rigorously evaluate the implementation of evidence-based quality measures to guide CRRT care matched with the clinical course of the critically ill patient.

Methods

The methodology of ADQI consensus meetings are well developed and have undergone refinement in the last 2 decades, as previously described [8]. The aim of ADQI is to provide expert-based statements, supported by evidence where applicable, and interpretation of current knowledge for use in clinical care by healthcare providers and decision-makers. In addition, ADQI aims to identify evidence care gaps to further establish research priorities. The 17th ADQI consensus meeting convened a diverse panel of experts representing the disciplines of nephrology, critical care, epidemiology, biostatistics and biomedical engineering around the theme of 'Continuous Renal Replacement Therapy' for a 3-day meeting in Asiago, Italy (June 10–13, 2016) [3].

The ADQI methodology begins with a pre-conference comprehensive literature search and appraisal of scientific evidence to identify key themes. The core theme for this work group centered on 'solute control in CRRT'. The work group summarized areas where there is consensus supported by evidence, consensus but limited or no evidence and existing knowledge gaps where consensus was uncertain. The work group identified 4 core themes to generate questions on for presentation to the ADQI delegates during the meeting (table 1). The work group iteratively developed and refined consensus statements in response to each core question. Core questions and statements were presented during 5 successive plenary sessions involving all ADQI delegates for debate, discussion, suggested revisions and final consensus. Following the conference, this summary review of the process and final content was generated, reviewed and approved by all work group members.

Review

Question 1: What is the ideal method to prescribe and measure delivered CRRT dose for solute control?

Consensus Statements
Prescription
(1) CRRT dose identifies the amount of blood cleared of solute by unit of time (Level III; Grade D).
(2) Effluent flow is an acceptable surrogate for prescribing CRRT dose for solute clearance. The clearance is dependent on the sieving coefficient of the representative solute (Level III; Grade D).
(3) Default prescribed CRRT dose should be 20–25 ml/kg/h for representative small molecular weight solutes. Urea is the solute most commonly used to quantify dose (Level III; Grade D).
(4) Prescribed dose is dynamic. This default prescribed dose can be modified according to patient demand and in response to iterative evaluation of quality measures. Prescribed dose should be evaluated at least once every 24 h and more often according to patient needs (Level V; Grade E).

Delivery
(5) Dose delivery can be estimated as intensity (ml/kg/h times the number of treatment hours) or as time-averaged (average ml/kg/h over 24 h or other duration) (Level III; Grade D).
(6) Dose delivery should be routinely reassessed and modified based on iterative evaluation of quality measures. Dose delivery should be evaluated at least once every 24 h often according to patient needs (Level V; Grade E).

Context
CRRT dose is most commonly defined by extracorporeal urea clearance [1]. Urea clearance (sieving coefficient ~1) is reasonably estimated by weight-based effluent flow rate (ml/kg/h) [9]. Urea is most commonly used as a surrogate for clearance of small solutes; however, it is not the only solute readily removed by CRRT. Extracorporeal solute clearance is dependent on solute molecular weight, sieving coefficient, membrane type and fouling and modality [10]. Conventional CRRT membranes efficiently remove small solutes. Larger molecules are better cleared with hemofiltration and in the first 12 h of filter use [11]. Small molecular weight solutes are not significantly affected by CRRT modality or progressive clotting of the membrane [11].

The Kidney Disease: Improving Global Outcome (KDIGO) CPG for AKI have recommended a default CRRT dose prescription (for urea clearance) of 20–25 ml/kg/h effluent flow rate, regardless the chosen modality or proportion of replacement fluid given pre or post filter [4, 12]. Recent data have shown that CRRT dose lower than recommended by the KDIGO CPG default dose can achieve adequate control of serum urea concentrations [13]. This study implies that providers can adjust or adapt the default CRRT dose based on the patient's clinical condition and need. Effluent flow rate can be increased or decreased in response to changes in clinical, physiologic and/or metabolic status. This may include targeting specific solutes and/or modification in response achieving benchmark targets from CRRT quality measures. Importantly, there are currently no data to support the concept that dynamic prescription improves surrogate or patient-centered outcomes. However, the rationale for dynamic prescription integrating audit and feedback from routine quality measures could theoretically better optimize solute control and quality of delivered CRRT [14].

We contend that CRRT dose delivery should be routinely monitored. Intensity may be a reasonable method to measure delivered dose [2]. Intensity is defined by the product of efficiency and time, where efficiency is the clearance measured in milliliters per kilogram per hour. Intensity represents the blood volume cleared of a solute after a certain period of time and can be expressed as milliliters or milliliters per kilogram. For example, prescribing 20 ml/kg/h to a 100 kg patient after 24 h of uninterrupted therapy should result in 480 ml/kg of intensity (or 48 liters in a 100 kg patient). If the actual result is less than 480 ml/kg of intensity due to treatment interruption or downtime, the effective delivered dose is less than the prescribed dose.

Alternatively, delivered dose can be calculated as time-averaged dose in milliliters per kilogram per hour over the 24-hour timeframe. For example, if a prescription of 20 ml/kg/h is applied for 12 h, then decreased to 15 ml/kg/h over the subsequent 6 h and interrupted thereafter (the next 6 h), the time-averaged dose will be the following: $((20 \times 12) + (15 \times 6) + (0 \times 6))/24 = 13.75$ ml/kg/h. This would represent a delivered dose below that of the intended level. This would represent suboptimal CRRT care. Effective delivered dose should be monitored routinely to ensure the prescribed CRRT is achieved [15] (fig. 1).

We recognize that CRRT dose is only one dimension of 'CRRT adequacy'. Accordingly, additional aspects of CRRT care should also be integrated and monitored in the broader clinical context of the patient's clinical status (i.e., timing, fluid removal, anticoagulation) [13].

Recommendations for Clinical Practice
A reference dose of 20–25 ml/kg/h can be reasonably recommended as the default prescription for CRRT dose in critically ill patients. This dose represents small mo-

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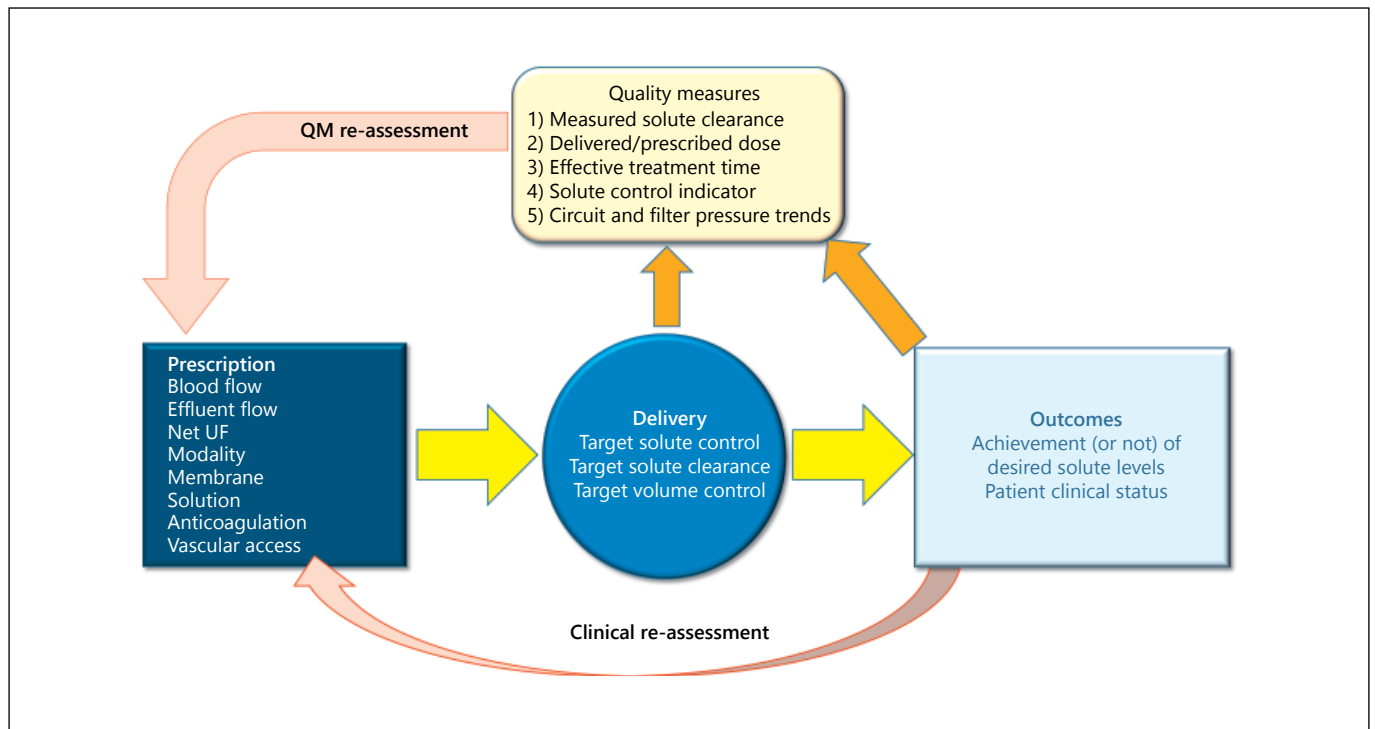
Fig. 1. Concept of dynamic CRRT dose. Following the initial prescription of CRRT, treatment begins which may modify patient course and outcome. At this point, providers should frequently reassess the response to prescribed CRRT dose. This can be achieved by following selected quality measures focused on CRRT dose. These quality measures could target delivered clearance; ratio of delivered to prescribed dose; effective treatment time; and other measures of solute control. Furthermore, the patient's clinical condition may change while receiving CRRT. In such circumstances, CRRT prescription may require additional modification (e.g., reduction or interruption of net ultrafiltration in response to hemodynamic deterioration and/or hypovolemia). Reprinted with permission from www.ADQI.org.

lecular weight solute clearance (e.g., urea) and should be modified according to the changing status of the patient. A critically important aspect to monitor for CRRT prescription is delivered dose. This should be monitored as a quality measure.

Recommendations for Research

We identified the following themes for future research:

- Future work should identify specific and/or novel target solutes for CRRT prescription and blood level control (e.g., middle molecular weight solutes, biomarkers etc.) [16].
- Future work should identify the optimal technique (indicated as the combination of membrane/modality/efficiency) in order to target specific solutes.
- Future work should identify the optimal timeframe for routine prescription re-evaluation.
- Future work should identify the optimal timeframe for routine intensity assessment.

Question 2: What are the effects of the delivered dose of CRRT on solute control?

Consensus Statements

(1) Delivered dose of CRRT is dynamic and affects the clearance of urea and other solutes. Clearance of such solutes may or may not be intended as part of the CRRT prescription. Examples of solutes initially targeted for removal include creatinine, potassium, phosphate, sodium, uric acid and ammonia (Level I; Grade A).

(2) Unintended removal of solutes can lead to potential adverse effects. Examples include excessive clearance of phosphate, potassium, magnesium, nutrients and medications (i.e., antimicrobials) (Level II; Grade B).

(3) Delivered CRRT dose affects the acid–base balance (Level I; Grade A).

(4) Solute clearance is further contingent on technological factors such as CRRT modality, membrane characteristics and CRRT operational characteristics (Level II; Grade B).
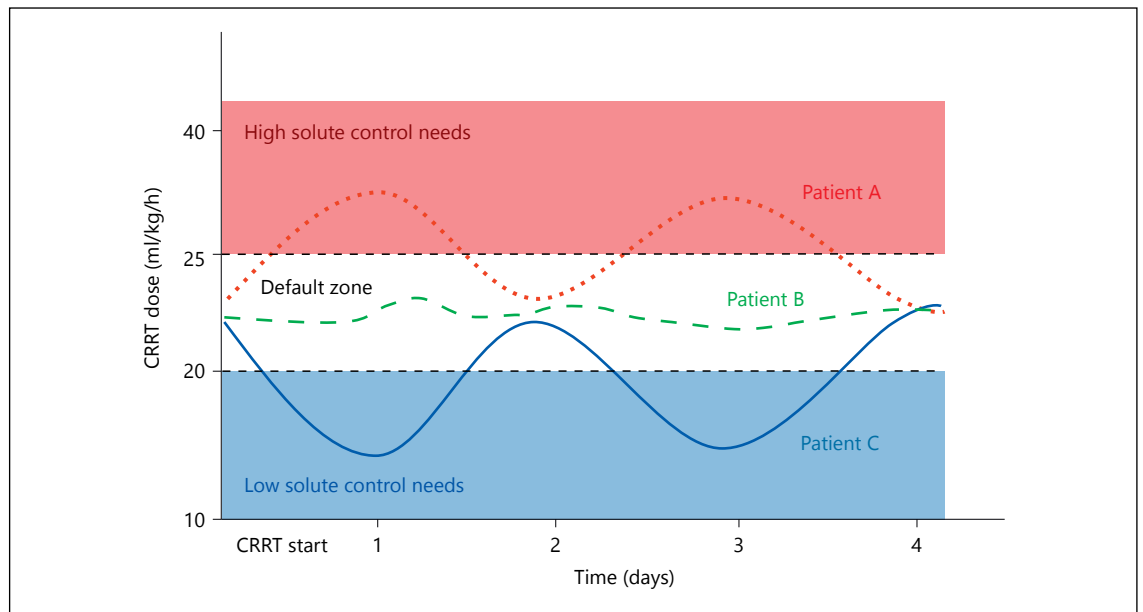
Fig. 2. Precision CRRT delivery. CRRT dose should be dynamic and adapted to changes in acuity, physiology and metabolic profile of critically ill patients. For example, patient A has pneumonia and oliguric AKI. The CRRT dose is increased from the default of 20–35 ml/kg/h after 24 h due to the development of a hypercatabolic state characterized by sepsis and increasing serum urea concentration. The next day, the patient's condition improves and urea control is achieved. The CRRT dose can now be reverted to 20 ml/kg/h. By day 3, the patient receives nutritional support which contributes to increasing serum urea concentrations at a CRRT dose of 20 ml/kg/h. This would again require dose modification. Alterna-tively, patient C has diuretic-resistant congestive heart failure and fluid overload. Following initial CRRT prescription primarily for fluid removal, solute clearance exceeds demand due to residual kidney function. Accordingly, the patient's CRRT dose is reduced to 15 ml/kg/h. By day 2, the patient's urine output decreases and serum urea concentration increases. In this circumstance, the prescribed CRRT dose can be increased to achieve the new solute control target. Finally, patient B is critically ill and is admitted to ICU following surgery. This patient achieves steady state solute control without the need for modification with the default CRRT dose of 20–25 ml/kg/h. Reprinted with permission from www.ADQI.org.

Context

The clearance of low molecular weight solutes during CRRT closely approximates total effluent flow. An effluent volume of 20–25 ml/kg/h is recognized as an accepted dose of CRRT in critically ill patients with AKI and represents urea clearance [4, 6, 7]. The prescription and delivery of CRRT dose affects other aspects of medical management, including correction of electrolyte and acid–base imbalance, volume control and clearance of other solutes and medications. Clearance of solutes such as creatinine, potassium, phosphate, sodium, uric acid and ammonia may be initially indicated based on the desired target level for the solute. However, a higher dose than 20–25 ml/kg/h may be indicated if the target level of a specific solute cannot be achieved. Similarly, a higher dose of CRRT may be required to maintain the acid–base homeostasis or to correct evolving acid–base disturbances. While the default initial CRRT dose recommendation of 20–25 ml/kg/h applies to the majority of critically ill patients, the CRRT prescription may need individualization and iterative reassessment with appropriate adjustments to achieve adequate fluid, electrolyte and metabolic balance (fig. 2).

CRRT delivered dose can also result in the clearance of unintended solutes, potentially contributing adverse events. CRRT can cause significant electrolyte derangements due to removal of solute from the blood without adequate replacement [17, 18]. Both hypophosphatemia and hypokalemia frequently complicate prolonged treatment. While initial phosphate removal may be indicated to achieve a biochemical target, continued removal can result in hypophosphatemia [6, 7, 19, 20]. Hypophosphatemia has been associated with respiratory muscle weakness, delayed ventilator weaning, myocardial dysfunction and rhabdomyolysis, as well as with other complications. Analogously, initial potassium removal may be indicated but continued removal can predispose to hypokalemia and cardiac dysrhythmias.

CRRT dose may also impact nutritional parameters and vital medication dosing. Since the CRRT readily

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clears low molecular weight water-soluble substances, significant loss of glucose, amino acids, low molecular weight proteins, vitamins and trace elements also occur [21, 22]. CRRT delivered dose also has the inadvertent consequence of increasing drug clearances and can result in the potential suboptimal dosing of antimicrobials [23, 24]. Therefore, the influence of CRRT dose must be taken into account when prescribing antimicrobials and other vital medications. CRRT modality, CRRT operational characteristics and membrane characteristics can affect the dose [2, 25, 26]. The clearance of 'middle' molecular weight solutes is greater for convective than diffusion-based techniques [27]. In convective therapies, the location of replacement fluid delivery in the extracorporeal circuit significantly impacts solute clearance. Replacement fluid can be infused prior to the filter (pre-filter) or after the filter (post-filter) in varying amounts. The use of post-filter [28] replacement fluid is limited by the filtration fraction due to increased clotting of the CRRT circuit. While addition of the replacement fluid pre filter can reduce the filtration fraction and likelihood of filter clotting, it also decreases solute clearance [12, 28]. High-flux, high cutoff and adsorptive membranes can increase removal of both middle and large molecular weight solutes [29].

Recommendations for Clinical Practice

In prescribing CRRT dose, additional parameters should be considered beyond urea clearance, such as acid–base and electrolyte homeostasis, nutrition, fluid balance and antimicrobial clearance. Monitoring of serum concentrations of target solutes, along with complications of delivered dose, should routinely be performed at least once every 24 h or more frequently based on patient need. CRRT prescription may require adjustment to achieve the physiologic target of these other solutes. At the same time, excessive clearance of electrolytes and other solutes such as nutrients may need to be supplemented. Patients on CRRT should have consultation with a critical care dietician to prescribe suitable nutritional support and a critical care pharmacist to perform dose adjustment of medications. Therapeutic drug monitoring should also be used when possible to ensure more accurate antibiotic therapy.

Recommendations for Research

We identified the following themes for future research:
- Future research should include the evaluation of other aspects of delivered CRRT dose including fluid management and acid–base and electrolyte balance.
- Future research should include assessment of the impact of non-CRRT fluids and solute administered on delivered dose.
- Rigorous evaluation of the appropriate dosing of antibiotics based on pharmacokinetic studies is needed since data are limited.
- Future research should include assessment of nutritional losses and the impact of supplementation on patient outcomes.

Question 3: Can precision modification of target CRRT dose tailored to evolving patient status contribute to improved patient outcome?

Consensus Statements
(1) CRRT dose should be dynamic and adapted to changes occurring in the acuity, physiology and metabolic profile of the critically ill patient. Critically ill patients are heterogeneous and vary widely in their demographics, chronic disease burden, case-mix and illness acuity (Level V; Grade E).
(2) Precision CRRT dosing should be adapted to target specific solutes (Level V; Grade E).

Context
We recognize that critically ill patients are a heterogeneous mix characterized by wide differences susceptibilities to AKI, its complications and outcome (e.g., metabolic derangement, acidosis, fluid overload) [30–32]. Critically ill patients vary in age, body weight and composition, burden of comorbid disease (in particular chronic kidney disease), case-mix and acute illness severity. Accordingly, a standard and fixed CRRT dose of 20–25 ml/kg/h may not be appropriate for critically ill patients whose course of critical illness may be marked by rapid changes in clinical, physiological and metabolic profile. While we believe current evidence would recommend a default CRRT dose of 20–25 ml/kg/h, we recognize that the prescription of CRRT may need to be dynamic. This introduces the concept of a patient-centered 'precision' approach to CRRT prescription. This would imply that CRRT dose would be modified over time to match the clinical demands of the patient (i.e., changes to kidney reserve, changes to illness severity, changes to non-renal organ dysfunction, changes to fluid balance and metabolic status) [33]. This would be analogous to how mechanical ventilation is prescribed in critically ill patients with acute lung injury.

For example, a hypercatabolic critically ill patient (e.g., burn injury or tumor lysis syndrome) may initially require

a greater CRRT dose than the default of 20–25 ml/kg/h to achieve acceptable solute control (i.e., azotemia and electrolyte derangement). As the patient's clinical status improves, the CRRT dose should naturally be reduced to 20–25 ml/kg/h. This default CRRT dose could be further decreased in a patient who starts to recovery kidney function characterized by increasing residual kidney function. An alternative example would be a critically ill patient with sufficient residual kidney function to maintain reasonable solute control, however requires CRRT for management of fluid overload. Such patients may not initially require the default CRRT dose of 20–25 ml/kg/h for solute unless they suffer further deterioration in kidney function.

We also recognize that CRRT dose may necessitate targeting of specific solutes relevant to the baseline and changing clinical status of the patient. For example, a critically ill patient with rhabdomyolysis may demand a greater CRRT dose, using convective therapies and a high cutoff membrane to clear high circulating concentrations of myoglobin. Similarly, critically ill patients who initialed achieved stable state solute control with the default CRRT dose of 20–25 ml/kg/h may suffer further deterioration marked by severe acidemia [34]. The prescribed CRRT dose would then need to be modified to control of acidosis.

Recommendations for Clinical Practice

Providers should recognize that the prescription of CRRT dose is dynamic and may need to be modified in response to patient factors such as baseline susceptibilities and reserve and changes in clinical status. Accordingly, CRRT dose should be customized and tailored to the specific demands of the individual patient.

Recommendations for Research

We identified the following themes for future research:
- Future work should integrate the changes in residual kidney function of patients receiving CRRT to guide optimal dose.
- Future work should evaluate candidate biomarkers and actionable levels of biomarkers to guide when to start CRRT and also when to potentially modify dose during the course of treatment.
- Future work should evaluate subgroups of critically ill patients where precision CRRT dose modifications may improve patient-centered outcomes such as survival and recovery of kidney function.

Question 4: What quality measures (quality indicators) should monitor dose and solute control in CRRT?

Consensus Statements

(1) Quality measures for CRRT should be implemented into the routine clinical application of CRRT (Level V; Grade E).
(2) Quality measures should specifically target CRRT dose prescription, delivery and solute control (Level V; Grade E).
(3) CRRT technology and bedside electronic health records (EHRs) should be leveraged to reliably and routinely calculate quality measures (Level V; Grade E).
(4) Quality measures, specifically benchmark targets, should be reported at both patient level and, in aggregate, at an operational level (Level V; Grade E).

Context

The quality of care for critically ill patients receiving CRRT has been recognized as a clinical and research priority [14]. Indeed, several organizations (i.e., ADQI, KDIGOs) have worked towards implementing evidence-based guidelines for CRRT care, improving the standards of care for patients receiving CRRT and identifying important knowledge gaps [35–37]. Despite these initiatives, there remain numerous challenges with respect to quality and safety in CRRT care.

CRRT is the predominant form of acute RRT provided to critically ill patients and its utilization is increasing [38]. CRRT is a therapeutic and support technology often applied to the most severely ill patients, often in the context of multiple organ dysfunction, and among those who are particularly prone to medical errors and adverse events [14]. CRRT is also relatively resource intensive, costly and requires specialized training to operate.

CRRT is also susceptible to considerable variation in practice. Such practice variation may contribute to independent risk for suboptimal quality of care and/or less favorable outcomes [15, 26, 39]. Such variation is likely multifactorial and has arisen from critical evidence care gaps to guide practice, heterogeneous providers (e.g., nephrology; critical) and differences in institutional expertise in CRRT. We also recognize there is a paucity of validated evidence-informed quality measures available to implement into routine practice to guide and monitor aspects of CRRT prescription and delivery [14, 15, 26, 39, 40]. This is a clear clinical and research priority.

The aim of integrating quality measures into routine clinical CRRT care is to standardize a default prescription, ensure greater reliability of CRRT delivery and target aspects for continuous quality improvement initiatives. We recognize that quality measures should be developed across a range of domains related to CRRT care

Table 1. Summary of core questions focused on 'solute control in CRRT'

Core questions for 'solute control in CRRT'
(1) What is the ideal method to prescribe and measure delivered CRRT dose for solute control?
(2) What are the effects of the delivered dose of CRRT on solute control?
(3) Are different target doses of CRRT needed at various stages of the patient condition?
(4) What quality measures (quality indicators) should monitor dose and solute control in CRRT?

Table 2. Summary of proposed quality measures for CRRT dose

Metric	Definition	Calculation	Benchmark target
Dose (clearance)	This QM focuses on solute clearance to determine delivered dose using blood and effluent solute concentration. This QM provides an instantaneous estimate of filter efficacy (i.e., sieving coefficient). This QM can be serially measured to evaluate solute clearance and filter performance. The default solute is urea; however, this QM could be applied to additional solutes	QM = effluent (urea)/blood (urea)	≥ 0.80
Dose (ratio of delivered/ prescribed)	This QM focuses on the effluent volume delivered relative to prescribed dose. This measure would be calculated as the ratio of average effective delivered dose (time-averaged (24 h)) divided by prescribed dose	QM = average effective delivered dose/prescribed dose	≥ 0.80
Effective treatment time	This QM focuses on the total average time a patient receives treatment in a given 24 h period. This measure is based on time and would incorporate treatment interruptions that were planned and unanticipated. Initial benchmark target should be $\geq$20 h/day. Additional QMs related to contributors and response to unplanned interruptions are necessary (e.g., catheter function, circuit/filter clotting, anticoagulation)	QM = 24 – downtime (hours)	≥ 20
Solute control indicators	This QM focuses on the absolute and/or relative change in targeted solutes that represent a target of CRRT prescription	QM = $\text{solute}_{Day(x+1)}/\text{solute}_{Day(x)}$	≤ 1.0
Circuit control indicators	This QM focuses on temporal trends in circuit and filter membrane pressures. These would specifically evaluate the pressure drop (P_{DROP}) and transmembrane pressure (TMP). These measures would indicate suboptimal clearance and risk of treatment interruption	QM = relative or absolute changes in P_{DROP} or TMP	P_{DROP}<? TMP<?

(e.g., personnel certification, center accreditation, prescription, delivery, anticoagulation, treatment interruptions, catheter-related, circuit-related) [40].

For this ADQI, we have specifically focused on quality measures for CRRT dose prescription, dose delivery and solute control [41, 42]. While proposed quality measures will target discrete aspects of CRRT dose, these should also be complementary. This would imply that no single quality measure can satisfy all the aspects of CRRT dose prescription and delivery (table 2).

We recognize the rapid expansion of electronic medical records, and adaptable bedside clinical informatics has provided opportunity for point-of-care calculation and display of CRRT quality measures. This can be made available to bedside providers caring for the patient (e.g.,

physicians, nurses). Quality measure data can also be utilized by members of allied health providers (e.g., pharmacists, dieticians) to guide the prescription and adjustment of medications (e.g., antimicrobials) and nutritional support (e.g., calories, protein, micronutrients). This represents an important mechanism to guide precision CRRT prescription, maximize compliance with evidence-informed care and achieve target benchmarks.

We have proposed 4 prototype quality measures to target variable aspects of CRRT dose: delivered clearance, ratio of delivered to prescribed dose, effective treatment time and solute control (table 2). Although CRRT is intended to function 24 h a day (analogous to a native kidney), treatment is often be interrupted [15, 26]. It is well established that unplanned interruption of treatment can

negatively impact CRRT efficiency and safety [15]. We propose that a quality measure should be focused on monitoring 'effective treatment time'. This would further be used to help discriminate whether treatment interruption was planned (e.g., scheduled filter changes, transfers to operating theatre, diagnostic imaging) or rather was unintended (e.g., catheter dysfunction, circuit/filter clotting, anticoagulation; table 2). We contend these quality measures could be reasonably integrated into routine care to guide individual patient CRRT. Moreover, we also contend that these quality measures (and achievement of target benchmarks) should be reported in aggregate at an operational level to facilitate broader quality improvement activities and improvement in CRRT-related operations management.

Quality measures should also be assimilated into larger clinical and/or administrative databases (i.e., data repositories or registries) or a specific CRRT quality registry should be built to further develop, validate and refine quality measures for the purpose of setting benchmark targets for experienced CRRT institutions and those establishing CRRT programs.

Recommendations for Clinical Practice

All institutions that provide CRRT should integrate, monitor and report quality measures for CRRT. Programs should set target benchmarks for each quality measure. Particular quality measures should be implemented for CRRT dose prescription, delivery and solute control, such as those proposed in table 2, ideally leveraged through bedside EHRs or derived directly from CRRT machine data.

Recommendations for Research

We identified the following themes for future research focused on quality measures in CRRT:
- Future work should rigorously develop, validate and prioritize specific quality measures for processes of care, treatment-specific end points, patient-centered outcomes and resource utilization for CRRT care.
- Future work should rigorously evaluate target benchmarks for each quality measure that can inform about patient-specific quality of care and aggregate institutional quality of care.
- Future resources should be directed toward developing a multicenter CRRT registry to further develop, validate and refine quality measures for implementation into routine practice and informing on ideal target benchmarks for integration into updated CPG.

Conclusions

Current CRRT dose is informed from high quality evidence suggesting no impact of static CRRT dose on patient outcomes; however, there is rationale for re-evaluation of CRRT dose to integrate the concept of dynamic solute control adapted to the changing clinical needs of critically ill patients. This concept of dynamic CRRT delivery should target both intended and unintended solute clearance. Quality measures specific for monitoring delivered CRRT dose have been proposed that require further validation prior to implementation into practice to guide optimal CRRT dose.

Disclosure Statement

S.M.B. and A.T. have consulted and received honoraria from Baxter Healthcare Corp.

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