

Acute Dialysis Quality Initiative

Workgroup 5

Operational Characteristics

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Introduction

The operational characteristics of the different modalities of continuous renal replacement therapy impact on the performance of these therapies. Major factors to be considered include the differences between therapies that provide predominantly convective solute clearance as compared to therapies that provide predominantly diffusive clearance, the role of arteriovenous versus venovenous therapies, the impact of modality selection on patient outcome, and the optimal components comprising a CRRT delivery system.

What are the operational characteristics of each CRRT modality?

HF (CVVH)

Continuous hemofiltration is characterized by predominantly convective solute transport. Some diffusive transport may occur as the result of concentration gradients established when sieving coefficients are significantly < 1 , however, the contribution of diffusion will be small relative to the convective component.¹ (Level V)

HD (CVVHD)

Continuous hemodialysis is characterized by predominantly diffusive solute transport, with convection occurring as a result of prescribed ultrafiltration and internal filtration/back-filtration. When hemodialyzers with high ultrafiltration coefficients are utilized for “high-flux” CVVHD, significant convective solute transport may occur from augmented filtration/back-filtration.¹ (Level V)

HDF (CVVHDF)

Continuous hemodiafiltration is characterized by mixed diffusive and convective solute transport.¹ (Level V)

How do we differentiate between HD (CVVHD) and HDF (CVVHDF)

Operationally, treatments are considered to be HDF when the amount of replacement fluids is prescribed as part of the CRRT prescription to replace ultrafiltration greater than desired fluid loss. (Level V)

What are the benefits of Convective vs. Diffusive therapies?

Membrane characteristics have a significant impact on solute removal. Convective and diffusive solute clearance can only be considered in the context of the individual membrane characteristics. However, some general statements can be made regarding convection and diffusion as relates to small and large molecule clearance, adsorption, drug clearances and outcome.

Impact on low MW solutes?

Several investigators have demonstrated relative equivalence between convective (CVVH) and diffusive (CVVHD) clearances for low MW solutes (using urea as the surrogate marker).²⁻⁵ Some of the variability in the reported data reflects variations in membrane characteristics. In particular, some membranes (e.g., certain polyamide membranes) are not designed for diffusive solute clearance.² (Level I)

Impact on middle/high MW solutes?

In general, convective transport will provide higher clearances for middle/high MW solutes than diffusive transport.^{3,4,6} Considerable variability based on membrane type has been observed. Factors influencing this variability include membrane thickness, pore size, membrane charge and adsorptive properties. (Level I)

Impact on adsorptive characteristics?

Data are inconclusive on the adsorptive ability of membranes for molecules that are considered pro-inflammatory mediators.⁷⁻¹⁰ PAN and polyamide membranes appear to be more adsorptive than membranes of polysulfone composition.⁸ Maximal adsorptive capacity appears to be rapid and membranes may reach saturation within hours of onset of blood membrane interaction.⁷⁻⁹ The clinical impact of membrane adsorption on circulating inflammatory mediator concentrations is speculative and is a source of ongoing research.¹⁰ (Level V)

Impact on drug clearance?

Drug clearance by CRRT is a function of multiple factors including molecular weight, percent protein binding, membrane composition and drug concentration in plasma.¹¹⁻¹⁴ For drugs with low molecular weight, clearance by convection and diffusion will be similar. As molecular weight increases, drug removal by diffusion declines to a greater extent than convective drug removal (assessed as the sieving coefficient of unbound drug, f_{up}). (Level I)

What is the impact of convection or diffusion on patient outcome?

There are no data comparing patient outcomes using convective (e.g, CVVH) and diffusive (e.g., CVVHD) therapies. Prospective randomized study of this issue is suggested.

Recommendations for clinical practice: Based on the available data, no recommendations regarding the use of predominantly convective therapies as compared to diffusive therapies can be made. Efficiency of removal of low molecular weight solutes is similar with convection and diffusion. Efficiency of middle and high molecular weight solute removal is greater with convective therapies, however data do not exist on the clinical implications of this enhanced solute removal. The clinical relevance of differences in solute adsorption is also unknown. Recommendations for future research: Randomized, controlled trials comparing convective and diffusive therapies need to be conducted to resolve whether one modality is preferable to another.

What is the impact of modality selection on patient outcome?

There are no data comparing patient outcomes for patients treated with continuous hemofiltration, continuous hemodialysis or continuous hemodiafiltration. No consensus exists as to which, if any, modality is superior.

How can the benefit of each form of CRRT be maximized?

For solutes?

Small solute clearance is generally proportional to hemofilter/ hemodialyzer effluent flow rate (Q_{D_0} or $Q_D + Q_{UF}$). For these solutes, clearance may be increased by increasing dialysate flow rate (Q_D) or by increasing ultrafiltration rate (Q_{UF}). In continuous hemodialysis, solute clearance is minimally affected by blood flow when the blood flow rate is greater than ~100 mL/min unless high volume (> 2.5 liters/hour) dialysate flow is utilized (Level II).²⁻³ In continuous hemofiltration, blood flow may need to be increased with increasing ultrafiltration rate in order to maintain an acceptable filtration fraction (Level V).

As solute molecular weight increases, the increase in diffusive clearance by increased dialysate flow diminishes. Augmentation of clearance may be achieved by increasing blood flow rate, by increasing ultrafiltration rate, by using a hemofilter/hemodialyzer with a higher ultrafiltration coefficient (increasing filtration/ backfiltration), or by using a hemodialyzer with greater surface area (Level V).²⁻³

For volume management?

Fluid removal (ultrafiltration rate) may be maximized by utilizing a hemofilter with a higher ultrafiltration coefficient, increasing hydrostatic pressure in the blood compartment, or increasing negative pressure in the dialysate compartment. Hydrostatic pressure in the blood compartment may be increased by increasing blood flow rate or by constricting the tubing post-filter. This latter strategy is not advocated, as it increases the risk of system thrombosis. In unpumped systems, ultrafiltrate compartment pressure may be reduced by

lowering the height of the collection bag or by applying negative pressure via pumps or vacuum suction (Level V).

What is the role of AV versus VV therapies?

The use of pump-driven systems has allowed the development of venovenous therapies. Although the use of blood pumps has increased the complexity of CRRT systems, there is general consensus that venovenous systems are the modality of choice.¹⁵⁻¹⁹ Venovenous therapies may be used in the pediatric population.¹⁸

Advantages of the arteriovenous therapies include ease of set-up and operation and low extracorporeal blood volumes. Disadvantages of arteriovenous therapies include the need for prolonged arterial cannulation, with attendant risks of arterial injury, hemorrhage and thrombosis, the requirement for a mean arterial BP > 60 mmHg to maintain satisfactory circuit blood flow, and the relatively low blood flows that can be achieved. As a result, the arteriovenous therapies cannot provide the higher clearances that can be achieved using venovenous therapy^{15,16} (Level III).

Among the advantages of the venovenous therapies are the decreased risk of vascular damage as compared to the arteriovenous therapies, the ability to maintain blood flow independent of mean arterial BP, the ability to achieve higher blood flow rates and the ability to achieve higher clearances^{15,16} (Level III).

Recommendations for clinical practice: When available, venovenous therapies are the preferred to arteriovenous therapies due to the ability to provide higher rates of solute clearance and the decreased risk of complications. Arteriovenous therapies should be reserved for settings in which venovenous therapy cannot be provided due to the absence of adequate equipment or personnel (Grade D).

Are there specific indications for HD vs HF vs HDF?

What are the factors that affect current practice?

Good epidemiological data describing current practice is not available, however, there are wide variations in local practice. There is no data to support any given modality as superior with regard to outcomes. Factors that may affect current practice include local availability of equipment, commercial availability of dialysis fluids and the lack of commercially available replacement fluid. Relative costs may play a significant role in local practice.

What are the theoretical issues?

In theory, choosing a CRRT modality that has a convective component should increase the middle molecule clearances. Whether this has an impact on clinical outcome is unknown. Depending on membrane characteristics, hemofilters adsorb cytokines and other sepsis-associated mediators (i.e. platelet-activating factor, tumor necrosis factor).^{5,20,21} The use of convective therapies may augment adsorption by rendering the entire thickness of the membrane available for this process.^{5,20,21} Adsorption may be limited

by rapid saturation of membrane binding-sites. However, clinical benefit associated with changes in cytokine levels has not been demonstrated²² (Level V).

What are the optimal components of a CRRT system?

Blood pump characteristics

The optimal characteristics of a blood pump will balance the degree of occlusion to promote forward motion of blood while having minimal impact on hemolysis. Factors influencing this include degree of occlusion, integrity of the pump segment of the blood tubing and duration of therapy. Recent literature does not re-evaluate these industry standards (Level V).

Ultrafiltration controllers

The move from adaptive CRRT machinery to industry produced CRRT machinery is in part for accuracy of ultrafiltration control. Intravenous pumps (which have a prescribed error rate of $\pm 5\%$ in the absence of a pressure gradient) have been found to have error rates as great as 30% when used to regulate ultrafiltration.^{23,24} Industry produced CRRT systems report ultrafiltration error rates of $\pm 1\%$ to ± 30 mls/hr. Using these “accepted” error rates will factor in as minimal or more significant depending upon the hemodynamics of the patient as well as the necessity of ultrafiltration accuracy for patient care (Level V).

Fluid balance regulation

The optimal fluid balance system would include a servo-regulatory system that balances hemofilter ultrafiltrate with dialysate flow and replacement fluid with low error rates thereby allowing for maintenance of desired fluid balance (Level V).

Pressure monitoring

Pressure monitoring in a pumped CRRT system is optimally measured immediately prior to and following the hemofilter to evaluate for pressure variation across the membrane. In addition, pressure monitoring of the access line prior to the blood pump permits should be performed in order to monitor catheter performance (Level V).

Safety monitoring

Air leak detectors and blood leak detectors are needed for safety (Level V).

Blood tubing

Blood pump tubing needs to withstand the prolonged occlusion and heat associated with repetitive motion of the roller segment (Level V).

Future innovations

Components not currently available on commercial CRRT that may benefit the clinical performance of these therapies include: capabilities for remote monitoring, plasma volume monitoring, closed-loop hemodynamic monitoring, solute monitoring, on-line production of substitution fluid and dialysate, and the development of plasma regeneration systems.

Discussion deferred

The workgroup deferred on discussion of issues regarding the appropriate personnel for the performance of CRRT. Specifically, the workgroup felt that there was no data to support the exclusive performance of these therapies by either intensivists or nephrologists, or by critical care or nephrology nurses. The workgroup believed that these decisions need to be resolved at individual healthcare facilities based on available resources and the local competency and credentialing of physicians and nurses. The criteria for this competency and credentialing have been addressed by medical and nursing professional societies.

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