1-1-2013

Considerations in the Critically Ill ESRD Patient

Balazs Szamosfalvi
Henry Ford Health, bszamos1@hfhs.org

Jerry Yee
Henry Ford Health, JYEE1@hfhs.org

Recommended Citation

Szamosfalvi B, Yee J. Considerations in the Critically Ill ESRD Patient. Advances in Chronic Kidney Disease 2013; 20(1):102-109.

Considerations in the Critically Ill ESRD Patient

Balazs Szamosfalvi and Jerry Yee

ESRD patients are admitted more frequently to intensive care units (ICUs) and have higher mortality risks than the general population, and the main causes of critical illness among ESRD patients are cardiovascular events, sepsis, and bleeding. Once in the ICU, hemodynamic stabilization and fluid-electrolyte management pose major challenges in oligoanuric patients. Selection of renal replacement therapy (RRT) modality is influenced by the outpatient modality and access, as well as severity of illness, renal provider experience, and ICU logistics. Currently, most patients receive intermittent hemodialysis or continuous RRT with temporary vascular access catheters. Acute peritoneal dialysis (PD) is less frequently utilized, and utility of outpatient PD is reduced after an ICU admission. Thus, preservation of current vascular accesses, while limiting venous system damage for future access creations, is relevant. Also, dosing of small-solute clearance with urea kinetic modeling is difficult and may be supplanted by novel online clearance techniques. Medication dosing, coordinated with delivered RRT, is essential for septic patients treated with antibiotics. A comprehensive, standardized approach by a multidisciplinary team of providers, including critical care specialists, nephrologists, and pharmacists, represents a nexus of care that can reduce readmission rates, morbidity, and mortality of vulnerable ESRD patients.

Key Words: Intermittent hemodialysis, Sustained low-efficiency dialysis, Online clearance monitor, Access recirculation monitor, Optical oxygen saturation sensor

Introduction

The incidence of developing dialysis-requiring ESRD is approximately 400 patients per million population in the United States.[1] ESRD patients are several fold more frequently hospitalized and admitted to the intensive care unit (ICU) than patients with normal kidney function. The major causes of admission to the ICU are sepsis,[2] particularly in patients on hemodialysis (HD) using a catheter access, and cardiovascular (CVS) events (eg, acute myocardial infarction, cardiac arrest, congestive heart failure, and cerebrovascular accident), with other common problems including HD access complications and gastrointestinal bleeding.[3] The most important causes of mortality are CVS events and sepsis.[1,4] When compared with patients with normal kidney function, ESRD patients in the ICU have an increased risk of mortality, mostly because of more severe comorbidity burden. ESRD survivors of an ICU admission often remain chronically ill after discharge and remain at a higher risk of mortality, new CVS events, malnutrition, and hospital re-admission for several months.[3,5-7] This review will discuss select aspects of caring for dialysis-dependent patients including the evolving concepts of measuring the delivered dialysis dose, ultrafiltration (UF) monitoring, and anticoagulation. Electrolyte and medication management issues were the subject of another recent review[8] and will be discussed only to a lesser extent here.

From the Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, MI.

Financial Disclosure: The authors are inventors of the automated regional citrate anticoagulation technology described in U.S. patents.

Address correspondence to Balazs Szamosfalvi, MD, Henry Ford Hospital, CFP-509, 2799 W. Grand Blvd, Detroit, MI 48202. E-mail: bszamos1@hfhs.org

1548-5595/$36.00

http://dx.doi.org/10.1053/j.ackd.2012.10.012

Assessment of the ESRD Patient in the ICU

In addition to the acute illness precipitating the ICU admission, ESRD patients may have a multitude of comorbidities, and it may be helpful if the nephrologist follows a comprehensive "checklist" on initial evaluation (Table 1). The ICU admitting diagnosis, evaluation, and treatment plan should be ascertained. The etiology and duration of ESRD; the outpatient dialysis modality and prescription; and any prior documentation of code status, end-of-life wishes, and circumstances under which dialysis withdrawal is desired should be assessed from the history and records. If residual kidney function is present, strategies should be used to preserve it, which is of particular importance in peritoneal dialysis (PD) patients. The hepatitis B surface antigen status should be established, and surface antigen-positive patients must be dialyzed in isolation with dedicated equipment. The PD catheter and exit site should be meticulously cared for by an experienced provider. The HD access should be examined daily for patency and signs of infection and, in the case of an arteriovenous fistula (AVF) or graft (AVG), the extremity should be protected from blood pressure cuffs, venipuncture, and the placement of an arterial catheter. This requirement should be emphasized to the ICU team and clearly documented in the patient's chart. The central veins draining the access arm should also be protected from venous catheters. The use of central venous catheters (CVCs) in the subclavian vein and of peripherally inserted CVCs via veins that could be used in the future for AVF or AVG creation should be avoided if possible. Ultrasound guided placement of a triple lumen CVC in the left internal jugular vein and preservation of the right internal jugular vein for HD access might be a practical approach that also avoids the use of femoral CVCs less preferred because of the increased risk of infection and thrombosis and decreased mobility. Systemic blood samples often can be

obtained during renal replacement therapy (RRT) or from the arterial catheter, reducing the need for venipuncture blood sampling. The extracellular and intravascular fluid volume status should be evaluated at least daily using a combination of physical examination, strict intake and output records, daily weight trends, and, when available, hemodynamic monitoring data trends. UF goals should then be established in close communication with the ICU team. The adequacy of small-solute clearance and electrolyte and acid-base control with dialysis should be monitored closely. The medication administration record must be reviewed daily and when the RRT prescription is changed to avoid the use of medications unsafe in ESRD (eg, succinylcholine, meperidine) and to ensure that drug dosing is adjusted for residual kidney function and delivered RRT. Antibiotic dosing in particular has to be coordinated with RRT and discussed frequently with the pharmacist. Medications unique to this population (eg, erythropoiesis stimulating agents, vitamin D compounds, and phosphate binders) should also be reviewed and used as warranted. Adequate nutrition should be ascertained daily, preferably by enteral feeding using a potassium- and phosphate-restricted formula or diet. Citrate-antibiotic dialysis catheter locking solutions are increasingly applied to prevent catheter infection. The ICU team should be warned to aspirate these before using the catheter during resuscitation to avoid temporary ionized hypocalcemia in the right atrium and ventricle. Finally, the appropriateness of continued aggressive ICU support in light of the patient's clinical course and previously stated advance directives (if available) should be evaluated periodically together with the ICU team and the patient or the surrogate decision-maker.

CLINICAL SUMMARY

- ESRD patients are more frequently admitted to the ICU and have a higher mortality than patients with normal kidney function.
- The delivered dose of hemodialysis may be monitored using online clearance to ensure correction of acid-base and electrolyte changes and inform antibiotic dosing in the ICU.
- Ultrafiltration goals should be defined together with the ICU team to achieve protocol-driven optimization of hemodynamics including central venous O_2 saturation.
- Novel dialysis systems with simple single-needle access and automated citrate anticoagulation may enable the safe use of sustained low-efficiency dialysis with arteriovenous fistula access in the future.

RRT

Dialysis Modality Selection

The proportion of ESRD patients maintained on PD may vary by country and region, resulting in varying utilization of PD in the ICU. Continued use of PD in the ICU may be difficult because of many factors, including the lack of cycler equipment and/or continuous ambulatory peritoneal dialysis (CAPD)-trained ICU nurses, particularly during nocturnal shifts. On the other hand, PD use in the ICU is prevalent and represents a successful, lower-cost alternative to extracorporeal blood purification in developing countries.[9] Usually, patients receive CAPD with 4-6 exchanges a day with volume in the range of 2-3 L adjusted to provide acceptable control of serum chemistry. However, continuing PD may be difficult or contraindicated in patients with severe Gram-negative, polymicrobial, or fungal peritonitis; in patients who require abdominal surgery; in patients with severe respiratory failure in which abdominal distension may further impair gas exchange; and in severely catabolic patients in which CAPD may not provide sufficient acid-base and electrolyte control. As a result, survival of the PD technique during and after an ICU stay is markedly limited.[10] Therefore, the remainder of this section will cover in more detail the more prevalent HD techniques used to support ESRD patients in the ICU.

Most ESRD patients are maintained on 3-times-a-week intermittent hemodialysis (IHD) as outpatients and stay on this modality when admitted to the ICU. IHD machines are designed to deliver 200-300 mL/minute diffusive urea clearance (Kurea) and operate at a blood flow (QB) of 300-500 mL/minute and a dialysate flow (QD) of 400-1000 mL/minute over a period of 3-5 hours.[11] Critically ill ESRD patients may not tolerate such intense therapy well, and the use of gentler, continuous renal replacement therapy (CRRT) may be considered. CRRT machines that use prepackaged, sterile dialysate and/or replacement fluids deliver 25-100 mL/minute diffusive and/or convective Kurea and operate at a QB of 100-300 mL/minute and a dialysate and/or replacement fluid flow of 25-100 mL/min 24 hours a day. Sustained low-efficiency dialysis (SLED) is a so-called hybrid therapy that is usually intermittent and uses an IHD machine to deliver 90-250 mL/minute diffusive Kurea operating at a QB of 200-300 mL/minute and a QD of 100-300 mL/minute over a prolonged period of 8-16 hours.[12]

Most ESRD patients rely on an AVF or AVG for HD access. This is cannulated with an arterial needle to withdraw uremic blood and a venous needle to return dialyzed blood to the patient during IHD, and the operator stays at the bedside to continuously monitor the patient. In the event of a return needle disconnect, life-threatening blood loss could occur in 2-5 minutes. There is no commercial technology that would provide 100% protection against this complication, although some recently approved monitoring systems may reduce the

Table 1. Problem-Focused Evaluation of the ESRD Patient in the ICU

Critical illness	Cause of admission to the ICU with evaluation and management plan.
ESRD history	Cause and duration of ESRD; hepatitis B surface-antigen status; outpatient dialysis prescription including outpatient urea kinetic volume of distribution (V), activated vitamin D and erythropoietin dose, code status, end-of-life wishes, and advance directives for dialysis withdrawal in ICU.
RRF protection	Particularly important in PD patients. Limit IV radiocontrast dye and nephrotoxic medication (eg, aminoglycoside) exposure as feasible.
Dialysis access	Assess for signs of infection. Document the patency of AVF or AVG daily. Ensure proper care of the PD catheter and exit site. Confirm that blood flow is sufficient to achieve the goals of therapy. ICU teams should avoid placing a blood pressure cuff, arterial- or central venous lines, or doing venipuncture on the access arm.
Vein preservation	Obtain blood samples with dialysis or from existing IV- or arterial lines to minimize venipuncture. Limit placement of peripherally inserted CVCs and subclavian venous catheters as feasible.
Volume status and UF	Assess patient weight and fluid intake and output at least daily. Monitor absolute value and trend of central venous pressure and central venous oxygen saturation ($ScVO_2$) as well as invasive arterial blood pressure and computerized pulse waveform analysis data when available.
IVFs	Use isotonic IVFs when possible. Calculate the hyponatremic effects of the free water load from certain IV antibiotics, vasopressors drips, and *N*-acetylcysteine infusions usually provided in 5% dextrose water.
Laboratory studies	Monitor at least daily chemistry profile, albumin, calcium, magnesium, phosphate, and complete blood count. Monitor blood cultures and cardiac laboratory tests as indicated.
Dialysis adequacy	Measure the delivered dose of small-solute clearance (OLC) with every IHD session and deliver at least 1.2 Kt/V (using outpatient or estimated V) 3 times per week. Provide extra treatments as needed for optimal volume and solute control.
Antibiotic dosing	Dose antibiotics in close coordination with the pharmacist, considering drug levels, residual kidney function, delivered small-solute clearance, and clearance of the drug with the modality of RRT and dialyzer utilized.
Other medications	Verify and adjust as needed the dose of blood pressure drugs, digoxin, seizure, and other medications with limited clearance in ESRD.

risk.[13] As a result, double-needle access of AVF and AVG cannot be recommended for safe use to provide either SLED or traditional CRRT in which the ICU nurse operator is not expected to stay at the bedside all of the time. In the absence of a clear survival advantage of CRRT over IHD (plus extrapolating from neutral studies in the acute kidney injury [AKI] population[14]) and considering the need for temporary catheter access for the former, ESRD patients with working AVF and AVG usually receive IHD in the ICU. ESRD patients with pre-existing HD catheter access may conveniently receive any RRT modality. In patients with AVF or AVG who have indications for CRRT (eg, severe hemodynamic instability on vasopressors, marked fluid overload requiring high daily cumulative fluid removal, or high risk of developing increased intracranial pressure [eg, with fulminant liver failure]) the possible complications of placing a temporary HD catheter to allow CRRT use must be weighed against the risks of continued use of IHD with the AVF or AVG. In the near future, machines with novel blood pumps[15] may become available enabling safe, single-plastic-needle access of AVF or AVG for 10- to 12-hour SLED. Compared with traditional CRRT, SLED is associated with important cost savings[16,17] and still allows for gentler solute and volume removal than IHD. Taken together, these developments may favor SLED over traditional CRRT and IHD use in ICU ESRD patients in the future.

Assessment of the Adequacy of HD in the ICU

In the AKI ICU literature, several recent, large, randomized, and controlled studies have failed to confirm that the delivered dose of small-solute clearance has an effect on survival in a broad dosing range once a minimally sufficient dose of uremic clearance is provided.[18,19] Likewise, a large, randomized, and controlled study in the stable outpatient HD population failed to show that increasing the dose of small-solute clearance beyond current Kidney Disease Outcomes Quality Initiative guidelines would lead to better survival.[20] Taken together, these data make it implausible that a simple escalation of delivered small-solute clearance beyond outpatient targets would lead to better outcomes in the critically ill ESRD patient. In the absence of strong evidence-based guidelines for small-solute clearance dosing targets in the ICU ESRD population, the authors believe that the recently published Kidney Disease: Improving Global Outcomes dosing guidelines for IHD and CRRT for ICU AKI patients[21] may also be applied as reasonable and simple dosing goals for ESRD patients.

However, different from the outpatient setting, ESRD patients in the ICU often require accurate dosing of life-saving medications (eg, antibiotics in sepsis), and measurement of the delivered solute clearance may become more relevant to outcomes if it is applied to the complex challenge of precisely dosing dialyzable drugs.[22,23] Further, when a life-threatening electrolyte disorder (eg,-severe hyperkalemia) or profound metabolic acidosis (eg, toxic alcohol ingestion) is diagnosed, being immediately able to measure the delivered small-solute clearance to confirm the efficacy of the RRT procedure in real time may be important and may allow for the detection of a dysfunctional, recirculating access sooner than possible

with the traditional method of analyzing serum chemistry trends on RRT.

Formal urea kinetic modeling, the gold standard of measuring the delivered dose of small-solute clearance during IHD in the outpatient setting, is difficult to perform in the ICU.[24] Traditional anthropomorphic equations[25] used to estimate the urea kinetic volume (V) usually do not correlate well with the much larger true V in the edematous, 10- to 20-L volume overloaded typical ICU patient. The urea generation rate may also be variable and usually increased in the critically ill catabolic patient.[26] Because ICU IHD and CRRT are not infrequently prescribed with no or reduced anticoagulation when compared with outpatient IHD, a gradual decline of the dialyzer performance during a single RRT session is possible and may also contribute to a delivered clearance lower than prescribed. All of these factors can be accounted for, and simplified equations can be used,[27] making urea kinetic modeling eventually feasible in expert academic settings.[28] However, the precise sampling and complex calculation requirements including possible considerations of cardiac output (CO) and systemic vascular resistance (SVR) in the regional blood flow model in critically ill patients may question the feasibility of this approach in routine clinical practice.[29]

Fortuitously, the delivered small-solute clearance can be measured automatically and without cost or risk to the patient using the online clearance (OLC) measurement available on several modern IHD machines.[11] The measurement requires dialysate flow above 300 mL/minute for the rapid modulation of the fresh dialysate sodium (Na) level in the range of 135-155 mEq/L and takes a few minutes to complete. The machine detects the electrical conductivity changes of the fresh and spent dialysate in response to the programmed changes in the fresh dialysate Na level. The way the technology is implemented on the market leader commercial dialysis machine limits the net amount of Na transferred between patient and dialysate to clinically negligible.[30] The effective ionic dialysance (Kecn; about equal to effective Na dialysance and effective urea clearance) is calculated in milliliters per minute; a decline of the dialyzer performance due to partial clotting and access recirculation (AR) reduce its value.[30] The blood temperature monitor (BTM; Fresenius) has multiple functions including measuring the temperature of the incoming and return limbs of the blood circuit to detect AR. For AR measurements, the IHD machine rapidly changes the temperature of the fresh dialysate, thereby indirectly changing the temperature of the venous return blood, and then senses any corresponding temperature change in the incoming blood that should only be observed if AR is present.[31] Correlating the online, automatically determined Kt with the apparent urea volume of distribution determined preferably with bioimpedance spectroscopy allows for the determination of the urea Kt/V with clinically sufficient accuracy and without the need for blood sampling and complex calculations.[32] OLC can also be obtained in 10-hour SLED using a commercial dialysis machine operating in IHD mode for 10 hours at a QB of 170 mL/minute and a QD of 400 mL/minute as recently shown by our group.[33] This approach will lessen the uncertainty about the delivered small-solute clearance during SLED, which made antibiotic dosing difficult and a plausible impediment to the wide adoption of the modality in the past.[34,35]

Finally, optical detection of ultraviolet-light-absorbing solutes in the waste dialysate with simple, low-cost technology was applied to indirectly monitor the delivered urea Kt/V in real time during IHD, and the technology is now available commercially.[36] Distinct from ionic dialysance, optical effluent sensing allows for continuous dialysate solute-level monitoring with immediate detection of changes. Application of this sensor to IHD and intermittent SLED in the ICU may be desirable, but it requires validation. However, because the Kt/V calculations rely on time-dependent reductions in effluent solute concentrations during intermittent therapy, the technology as described would be inapplicable during 24-hour CRRT with constant effluent solute levels in steady state.

In summary, ascertaining the delivered dose of small-solute clearance is feasible now with commercially available OLC technology. Further research in the ICU ESRD population is needed to confirm if OLC can be used to guarantee the delivery of a minimum dose of dialysis equivalent to the Kidney Disease Outcomes Quality Initiative-recommended outpatient 3-times-per-week 1.2 Kt/V HD dose, to immediately detect ineffective dialysis due to AR or partial dialyzer clotting, especially when patients with emergent electrolyte and acid-base changes are treated, and to precisely estimate the dialytic removal of important medications, particularly of drugs for which laboratory measurements are not readily available.

Once the delivered Kt/V is measured, the optimal fresh dialysate Na, potassium (K), and bicarbonate concentration may be adjusted during the RRT session, taking into consideration the patient's kinetic volume and predialysis chemistry and the rate of development of hyperkalemia and acidosis (or in rare clinical scenarios alkalosis) to result in an optimal postdialysis serum electrolyte profile. Generally, postdialysis hypokalemia and metabolic alkalosis should be avoided to lessen the risk of cardiac arrhythmias; therefore, when a large Kt/V is delivered (eg, with prolonged IHD or SLED), fresh dialysate Na, bicarbonate, and K levels should approximate normal plasma chemistry values. It may also be prudent to use a fresh dialysate Na level (possible range on the market leader dialysis machine 130-155 mEq/L) within 10 mEq/L of the patient's predialysis serum Na concentration to avoid an unduly large magnitude and rapid rate of correction of preexisting hyponatremia or hypernatremia, which may also be predicted based on

estimates of total body water and online-measured electrolytic conductivity clearance (Kecn).[37] ESRD patients with serum Na below 120 or above 165 meq/L are rarely encountered; such patients initially may require CRRT with custom-prepared replacement fluid Na levels to avoid unduly rapid correction of their severe dysnatremias. A fair estimate of the bicarbonate delivery during RRT may also be calculated from the delivered ionic dialysance and the average bicarbonate gradient between the patient's systemic plasma and the fresh dialysate. This information may be important to the ICU team to clearly define the severity of ongoing metabolic acidosis, which may be completely masked by several hundred millimoles of bicarbonate provided by the RRT session. The most common example is the development of lactic acidosis during SLED; this sometimes may go unnoticed unless the anion gap is corrected for hypoalbuminemia and trended and/or a dedicated lactate measurement is ordered.

Hemodynamic Optimization including Fluid Therapy and UF

Fluid Administration to ESRD Patients

ESRD patients admitted to the ICU may have low effective arterial blood volume and hemodynamic instability due to any combination of cardiac dysfunction, sepsis, severe liver disease, gastrointestinal bleeding, volume depletion, and third spacing after extensive surgery with or without overall extracellular fluid (ECF) volume reduction. Restoration of intravascular volume and circulation may require the administration of large volumes of intravenous fluids (IVFs). In the absence of ESRD patient-specific guidelines, the authors believe it is reasonable to assume that the principles of early goal-directed therapy[38] may also be applicable to the ESRD population with the obvious caveat that excess fluid infusion is more difficult to correct in anuric patients. However, by definition, anuric ESRD patients are unable to regulate their ECF tonicity without urine output, and even patients who have RRF are unlikely to be able to generate a significant medullary osmotic gradient and thereby variable urine tonicity. Therefore, to maintain a normal serum Na concentration and tonicity, the use of isotonic IVFs is usually required. In these patients, the effect on an ECF Na concentration of 1 L of IVF gained or 1 L of body fluid lost with a specific Na and K content can be reliably calculated and predicted.[39,40] The hyponatremic effect of hypotonic infusions (eg, vasopressors, *N*-acetylcysteine) and certain antibiotics administered in 5% dextrose-water IVF commonly used in the ICU should be predicted and if needed mitigated with the use of a higher Na fresh dialysate. When such calculations are omitted (eg, when a small ESRD patient receives 5-6 L of 0.45% half-isotonic saline perioperatively), clinically dangerous hyponatremia will develop, inexorably necessitating emergent dialytic correction. Even when ECF expansion is achieved while maintaining normotonicity, it is very difficult clinically to avoid "overshoot" and the development of varying degrees of ECF overload with or without pulmonary congestion in this usually anuric population. Finally, even if meticulous attention is paid to hemodynamic monitoring during IVF administration, pulmonary edema may develop with the resolution of the initial systemic inflammatory response syndrome (SIRS) causing rapid mobilization of third-spaced ECF volume, again requiring extra session(s) of or CRRT.

Hemodynamic Assessment to Guide UF Goals

Fluid overload may be present on ICU admission or may complicate the fluid therapy of critical illness in ESRD patients, and fluid overload is known to be associated with poor clinical outcomes in AKI.[41] A major goal of kidney support is to reduce the extracellular volume expansion with UF. However, it is very difficult to do this safely without compromising organ perfusion because patients are often hemodynamically unstable with insufficient intravascular refill rates that can fluctuate dramatically.[42] To guide IVF use, ICU teams often place catheters in the internal jugular vein with ultrasound guidance to monitor the absolute value and the trend of the superior vena cava O_2 saturation ($ScVO_2$) and central venous pressure in preference to the prior practice of using pulmonary artery catheters. The $ScVO_2$ is generally accepted as a useful, dynamic, surrogate marker of CO at unchanged arterial O_2 content and body O_2 consumption, with a lower value signifying a lower CO state.[43] $ScVO_2$ has also been associated with outcomes and complications after major surgery,[44] and optimization of $ScVO_2$ is a component of early goal-directed therapy for SIRS.[38] Computerized arterial pressure waveform analysis on dedicated devices may complement such monitoring because an arterial pressure line is usually in place in these patients. Obtaining a two-dimensional echocardiogram to define right and left ventricular systolic function, to detect and grade valvular heart disease, and to assess the presence of a pericardial effusion is noninvasive and may prove very helpful.

UF with Online Monitoring

Rapid net UF during IHD can lead to variable degrees of hemoconcentration and a corresponding relative reduction in the circulating blood volume with the ultimate development of hypotension and organ hypoperfusion. It is possible to detect this phenomenon in real time by integrating a low-cost, disposable optical chamber into the dialysis blood circuit prefilter and using a commercial optical hematocrit, relative blood volume, and O_2 saturation monitor. A pulse oxymeter-like sensor clips onto the

chamber from the outside and measures blood absorption of transmitted light at multiple wavelengths. The device calculates and displays the hematocrit, the hemoglobin level, and the O_2 saturation of the circuit incoming blood in real time. When the dialysis catheter tip is in the superior vena cava, the monitor essentially displays the $ScVO_2$ online at a negligible cost compared with a dedicated $ScVO_2$ monitoring catheter and device, and it may help to reduce net UF rates that are not tolerated before dangerous hemodynamic compromise develops. Conversely, blood volume monitoring was not useful to predict hypotension in the ICU,[45] but it could help detect catastrophic overultrafiltration, which rarely can and does happen due to operator error or equipment malfunction.[46] It is important to note that reliable readings during IHD and SLED may require very effective anticoagulation to prevent biofouling of the optical chamber. Once it develops, intradialytic hypotension may be treated by reducing the hourly net fluid removal rate and by small IVF or albumin boluses. The use of a slightly colder fresh dialysate temperature of approximately 35.0-35.5°C during IHD may also help lessen the incidence of hypotension by providing a mechanism to maintain the core temperature of the patient without the need for skin vasodilatation and increased perfusion for heat loss through radiation to the environment. Conversely, heat loss from the blood circuit during SLED and CRRT is essentially guaranteed because of the lower blood and dialysate or replacement fluid flows. Therefore, the use of a dialysate temperature below 36.5°C (including CRRT without a fluid warmer) is not recommended because it may lead to clinically significant hypothermia and mask a febrile state.

Anticoagulation During IHD, SLED, or CRRT

ESRD patients are at increased risk of bleeding in the ICU because of uremic platelet dysfunction and the possible presence of recent surgical wounds or gastrointestinal arteriovenous malformations. For brief (3- to 5-hour) IHD anticoagulation-free treatment sessions, saline flushes of the blood circuit may suffice. Use of acid concentrates with a final 1X dialysate content of 2.4-3 mEq/L citric acid as opposed to 3-4 mEq/L acetic acid may also have a modest anticoagulant effect. However, when using citric-acid-based dialysate, a 0.5-mEq/L higher dialysate calcium content may be necessary to achieve the same systemic ionized calcium level as with a 3- to 4-mEq/L acetic-acid-based dialysate.[47] Less thrombogenic blood circuits, catheters, and dialyzers incorporating novel surface-modifying macromolecules[48] and airless, nonturbulent blood flow pathways are in development and may be helpful in the future.

When an anticoagulant is necessary, the use of unfractionated heparin may be attempted because it is relatively short-acting and its effect can be reversed. Many other anticoagulants have been used during ICU dialysis and were recently reviewed.[49] However, all of these drugs, including heparin, have significant side effects and most importantly can increase the risk of systemic bleeding.

Regional citrate anticoagulation (RCA) is a very effective method to prevent clotting of the extracorporeal blood circuit without any systemic bleeding tendency. The procedure has gradually gained ground for CRRT and has been applied during IHD and 8- to 10-hour SLED.[17,50] RCA is now recommended in the Kidney Disease: Improving Global Outcomes Clinical Practice Guideline for Acute Kidney Injury as the method of choice for anticoagulation of CRRT circuits when citrate use is not contraindicated.[21] However, RCA use in nonexpert centers has been limited by concerns about severe electrolyte complications including hypercalcemia or hypocalcemia, hypernatremia, metabolic alkalosis, or acidosis, particularly in patients with shock and severe liver dysfunction. These complications were noted less frequently when RCA was used during intermittent SLED[17,50] and the principles of safe, near-automated delivery of RCA for IHD and SLED were described.[51] In our large ICU RRT program serving 160 ICU beds in a single center, we have been using 10- and 24-hour SLED-RCA protocols safely for many ESRD patients with catheter access even in the presence of severe liver dysfunction and/or shock.[33] Citrate accumulation and electrolyte abnormalities due to RCA are not observed, and clotting of the extracorporeal circuit is virtually never seen. In the future, 10-hour SLED-RCA may also increase the use of single-needle access of AVF and AVG in the ICU by eliminating the clotting risk inherent to the intermittent circuit blood flow.[52]

Quality Improvement Initiatives

ICU Dialysis Telemetry

In outpatient HD, telemetry collection of dialysis machine data during treatment is becoming mandatory in the United States. For example, one of the largest outpatient dialysis providers has been collecting online small-solute clearance data from its units as a proposed adequacy assessment and targeting tool for about a decade.[53,54] Computer and software technology developed for this purpose are easily adaptable to monitor IHD and SLED treatments provided in the ICU to ESRD patients.[33] Such data collection could confirm the duration of RRT, the delivered small-solute clearance, and the frequency and cause of machine alarms leading to treatment interruptions. This would be of obvious interest in the ICU, where considerably more variation in patient condition, treatment prescriptions, and complications occurs than in the outpatient setting. The wirelessly collected data can be stored on secure servers and used in real-time and post hoc quality monitoring and quality

improvement projects; we are now implementing such a program.[33]

Communication Between Providers

The importance of daily, detailed communication between the ICU team and the pharmacist was discussed earlier. A detailed report to the outpatient nephrologist about the hospital course and postdischarge care plan is also indispensable. ESRD patients may experience marked weight loss after a protracted ICU stay, which must be communicated for an immediate lowering of the estimated dry weight used in the outpatient dialysis center to correctly set net UF goals and prevent volume overload due to the use of an outdated, higher estimated dry weight. Conversely, patients may be discharged still recovering from SIRS with reduced blood pressure medications and significant ECF overload from earlier IVF therapy. Such patients may need daily outpatient HD for a few days for volume control and a gradual increase in blood pressure medications as they recover fully. Antibiotic therapy started in the ICU is often completed with postdialytic dosing in the outpatient HD unit. Detailed communication of the indication, duration, and dose of each agent is indispensable for optimal care. Changes to the outpatient medication regimen (eg, antihypertensive pills after an admission for uncontrolled hypertension) must also be communicated to allow the HD unit to monitor the effects of and compliance with the new drug schedule.

Discharge Planning to Prevent Re-Admissions

ESRD patients have an increased risk of mortality after the survival of an ICU admission, and in the United States the 30-day hospital re-admission rate of ESRD patients is very high at 36%.[1,55] Communicating in simple terms to the patient and family the cause of the hospital admission and the main treatment received is important for compliance with the care plan after discharge. In particular, compliance with the outpatient dialysis, diet, and adjusted medication regimen must be emphasized. Access to follow-up with the primary doctor and adequate insurance coverage and financial means to obtain the prescribed medications should be ascertained. Postdischarge follow-up phone calls and a home visit by a nurse can also help monitor and ensure patient compliance with the discharge plan.

Summary

ESRD patients are frequently admitted to the ICU, and their management poses many unique challenges. Meticulous attention to IVF therapy, optimization of hemodynamic status, medication dosing, and sophisticated use of multiple RRT strategies are all important elements of critical care support. Recognizing the higher risk of subsequent morbidity and mortality in ESRD patient ICU survivors and developing a comprehensive, multidisciplinary team strategy during the ICU stay and the discharge process may help improve outcomes and reduce hospital re-admissions.

References

1. U.S. Renal Data System. *USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2011.
2. Manhes G, Heng AE, Aublet-Cuvelier B, Gazuy N, Deteix P, Souweine B. Clinical features and outcome of chronic dialysis patients admitted to an intensive care unit. *Nephrol Dial Transplant.* 2005;20(6):1127-1133.
3. Strijack B, Mojica J, Sood M, et al. Outcomes of chronic dialysis patients admitted to the intensive care unit. *J Am Soc Nephrol.* 2009;20(11):2441-2447.
4. Herzog CA, Li S, Weinhandl ED, Strief JW, Collins AJ, Gilbertson DT. Survival of dialysis patients after cardiac arrest and the impact of implantable cardioverter defibrillators. *Kidney Int.* 2005;68(2):818-825.
5. Dara SI, Afessa B, Bajwa AA, Albright RC. Outcome of patients with end-stage renal disease admitted to the intensive care unit. *Mayo Clin Proc.* 2004;79:1385-1390.
6. Hutchison C, Crowe A, Stevens P, Harrison D, Lipkin G. Case mix, outcome and activity for patients admitted to intensive care units requiring chronic renal dialysis: a secondary analysis of the ICNARC Case Mix Programme database. *Crit Care.* 2007;11(R50): 1-14.
7. Uchino S, Morimatsu H, Bellomo R, Silvester W, Cole L. End-stage renal failure patients requiring renal replacement therapy in the intensive care unit: incidence, clinical features, and outcome. *Blood Purif.* 2003;21(2):170-175.
8. Arulkumaran N, Montero RM, Singer M. Management of the dialysis patient in general intensive care. *Br J Anaesth.* 2012;108(4): 183-192.
9. Ponce D, Berbel MN, Regina de Goes C, Almeida CT, Balbi AL. High-volume peritoneal dialysis in acute kidney injury: indications and limitations. *Clin J Am Soc Nephrol.* 2012;7(6):887-894.
10. Khan A, Rigatto C, Verrelli M, et al. High rates of mortality and technique failure in peritoneal dialysis patients after critical illness. *Peritoneal Dial Int.* 2012;32(1):29-36.
11. Polaschegg HD. Hemodialysis machine technology: a global overview. *Expert Rev Med Devices.* 2010;7(6):793-810.
12. Marshall MR, Golper TA. Low-efficiency acute renal replacement therapy: role in acute kidney injury. *Semin Dial.* 2011;24(2):142-148.
13. Polaschegg HD. Venous needle dislodgement: the pitfalls of venous pressure measurement and possible alternatives, a review. *J Ren Care.* 2010;36(1):41-48.
14. Rabindranath K, Adams J, Macleod AM, Muirhead N. Intermittent versus continuous renal replacement therapy for acute renal failure in adults. *Cochrane Database Syst Rev.* 2007;3:CD003773.
15. Shu F, Parks R, Maholtz J, Ash S, Antaki JF. Multimodal flow visualization and optimization of pneumatic blood pump for sorbent hemodialysis system. *Artif Organs.* 2009;33(5):334-345.
16. Ahmed Z, Gilibert S, Krevolin L. Cost analysis of continuous renal replacement and extended hemodialysis. *Dial Transplant.* 2009;38(12): 500-503.
17. Berbece AN, Richardson RM. Sustained low-efficiency dialysis in the ICU: cost, anticoagulation, and solute removal. *Kidney Int.* 2006;70(5):963-968.
18. Bellomo R, Cass A, Cole L, et al. Intensity of continuous renal-replacement therapy in critically ill patients. *New Engl J Med.* 2009; 361(17):1627-1638.

19. VA/NIH Acute renal failure trial network. Palevsky PM, Zhang JH, O'Connor TZ, et al. Intensity of renal support in critically ill patients with acute kidney injury. *New Engl J Med.* 2008;359(1):7-20.
20. Eknoyan G, Beck GJ, Cheung AK, et al. Hemodialysis Study Group. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *New Engl J Med.* 2002;347(25):2010-2019.
21. Kidney Disease, Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl.* 2012;2:1-138.
22. Heintz BH, Matzke GR, Dager WE. Antimicrobial dosing concepts and recommendations for critically ill adult patients receiving continuous renal replacement therapy or intermittent hemodialysis. *Pharmacotherapy.* 2009;29(5):562-577.
23. Mueller BA, Scoville BA. Adding to the armamentarium: antibiotic dosing in extended dialysis. *Clin J Am Soc Nephrol.* 2012; 7(3):373-375.
24. Schiffl H. Utility of urea kinetic modelling for prescription of adequate intermittent dialysis in critically ill maintenance dialysis patients. *Nephrol Dial Transplant.* 2007;22(7):2096.
25. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am J Clin Nutr.* 1980;33(1):27-39.
26. Marshall MR, Golper TA, Shaver MJ, Alam MG, Chatoth DK. Urea kinetics during sustained low-efficiency dialysis in critically ill patients requiring renal replacement therapy. *Am J Kidney Dis.* 2002; 39(3):556-570.
27. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol.* 1993;4(5):1205-1213.
28. Kanagasundaram NS. Prescription of an intermittent haemodialysis dose using urea kinetic modelling is feasible in the critically ill patient. *Nephrol Dial Transplant.* 2008;23(3):1075.
29. Kanagasundaram NS, Greene T, Larive AB, Daugirdas JT, Depner TA, Paganini EP. Dosing intermittent haemodialysis in the intensive care unit patient with acute renal failure—Estimation of urea removal and evidence for the regional blood flow model. *Nephrol Dial Transplant.* 2008;23(29):2286-2298.
30. Gotch FA, Panlilio FM, Buyaki RA, Wang EX, Folden TI, Levin NW. Mechanisms determining the ratio of conductivity clearance to urea clearance. *Kidney Int Suppl.* 2004;89:S3-S24.
31. Locatelli F, Buoncristiani U, Canaud B, Köhler H, Petitclerc T, Zucchelli P. Haemodialysis with on-line monitoring equipment: tools or toys? *Nephrol Dial Transplant.* 2005;20(1):22-33.
32. Lindley EJ, Chamney PW, Wuepper A, Ingles H, Tattersall JE, Will EJ. A comparison of methods for determining urea distribution volume for routine use in on-line monitoring of haemodialysis adequacy. *Nephrol Dial Transplant.* 2009;24(1):211-216.
33. Szamosfalvi B, Frinak S, Yee J. Sensors and hybrid therapies: a new approach with automated citrate anticoagulation. *Blood Purif.* 2012; 34(2):80-87.
34. Bogard KN, Peterson NT, Plumb TJ, Erwin MW, Fuller PD, Olsen KM. Antibiotic dosing during sustained low-efficiency dialysis: special considerations in adult critically ill patients. *Crit Care Med.* 2011;39(3):560-570.
35. Roberts JA, Mehta RL, Lipman J. Sustained low efficiency dialysis allows rational renal replacement therapy, but does it allow rational drug dosing? *Crit Care Med.* 2011;39(3):602-603.
36. Uhlin F, Fridolin I, Magnusson M, Lindberg LG. Dialysis dose (Kt/V) and clearance variation sensitivity using measurement of ultraviolet-absorbance (on-line), blood urea, dialysate urea and ionic dialysance. *Nephrol Dial Transplant.* 2006;21(8):2225-2231.
37. Pozzoni P, Di Filippo S, Pontoriero G, Locatelli F. Effectiveness of sodium and conductivity kinetic models in predicting end-dialysis plasma water sodium concentration: Preliminary results of a single-center experience. *Hemodial Int.* 2007;11(2):169-177.
38. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *New Engl J Med.* 2001;345(19):1368-1377.
39. Adrogue HJ, Madias NE. Hyponatremia. *New Engl J Med.* 2000;342(21):1581-1589.
40. Adrogue HJ, Madias NE. Hypernatremia. *New Engl J Med.* 2000;342(20):1493-1499.
41. Bouchard J, Soroko SB, Chertow GM, et al, Program to improve care in acute renal disease (PICARD) Study Group. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int.* 2009;76(4):422-427.
42. Doshi M, Murray PT. Approach to intradialytic hypotension in intensive care unit patients with acute renal failure. *Artif Organs.* 2003;27(9):772-780.
43. Marx G, Reinhart K. Venous oximetry. *Curr Opin Crit Care.* 2006;12(3):263-268.
44. Collaborative Study Group on Perioperative $ScVO_2$ Monitoring. Multicentre study on peri- and postoperative central venous oxygen saturation in high-risk surgical patients. *Crit Care.* 2006;10(6):R158.
45. Tonelli M, Astephen P, Andreou P, Beed S, Lundrigan P, Jindal K. Blood volume monitoring in intermittent hemodialysis for acute renal failure. *Kidney Int.* 2002;62(3):1075-1080.
46. Ronco C, Ricci Z, Bellomo R, Baldwin I, Kellum J. Management of fluid balance in CRRT: a technical approach. *Int J Artif Organs.* 2005; 28(8):765-776.
47. Gabutti L, Lucchini B, Marone C, Alberio L, Burnier M. Citrate- vs. acetate-based dialysate in bicarbonate haemodialysis: consequences on haemodynamics, coagulation, acid-base status, and electrolytes. *BMC Nephrol.* 2009;10:7.
48. Massa TM, Yang ML, Ho JY, Brash JL, Santerre JP. Fibrinogen surface distribution correlates to platelet adhesion pattern on fluorinated surface-modified polyetherurethane. *Biomaterials.* 2005;26(35):7367-7376.
49. Davenport A. What are the anticoagulation options for intermittent hemodialysis? *Nat Rev Nephrol.* 2011;7(9):499-508.
50. Clark JA, Schulman G, Golper TA. Safety and efficacy of regional citrate anticoagulation during 8-hour sustained low-efficiency dialysis. *Clin J Am Soc Nephrol.* 2008;3(3):736-742.
51. Szamosfalvi B, Frinak S, Yee J. Automated regional citrate anticoagulation: technological barriers and possible solutions. *Blood Purif.* 2010;29(2):204-209.
52. Buturovic-Ponikvar J, Gubensek J, Ponikvar R. Citrate anticoagulation for single-needle hemodialysis: safety and efficacy. *Ther Apher Dial.* 2005;9(3):237-240.
53. Lowrie EG, Li Z, Ofsthun N, Lazarus JM. The online measurement of hemodialysis dose (Kt): clinical outcome as a function of body surface area. *Kidney Int.* 2005;68(3):1344-1354.
54. Lowrie EG, Li Z, Ofsthun NJ, Lazarus JM. Evaluating a new method to judge dialysis treatment using online measurements of ionic clearance. *Kidney Int.* 2006;70(1):211-217.
55. Sood MM, Roberts D, Komenda P, et al. End-stage renal disease status and critical illness in the elderly. *Clin J Am Soc Nephrol.* 2011;6(3): 613-619.