Acute renal failure (ARF) is a common complication in critically ill adult patients in critical care units. ARF is defined as a sudden decline or cessation of renal function. Characteristics include inability of the kidneys to excrete wastes and maintain fluid, electrolyte, and acid-base balance. Despite advances in treatment, data from the past several decades continue to indicate that ARF still is associated with high mortality rates, ranging from 25% to 90%. Factors that may influence the rates include the increasing age of patients and the existence of comorbid conditions (eg, diabetes, preexisting renal disease, vascular disease). Historically, the treatment of ARF has been supportive. The primary focus of intermittent hemodialysis is to replace renal function by removing excess water and wastes. The standard of care for patients treated with intermittent hemodialysis may not be applicable to critical care patients because of the nature of the latter patients’ illness and catabolic state, the presence of systemic inflammatory syndrome with or without sepsis, and other organ failure. In this article, we review treatment of ARF in critically ill patients, indications for intermittent hemodialysis and continuous renal replacement therapy (CRRT), and the use of other variations of CRRT currently under investigation.

Management of ARF
Medications
ARF can be managed in some patients by nondialytic interventions such as loop diuretics (furosemide and bumetanide). Recently, the effect of diuretics in critically ill patients

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with ARF has been questioned. Mehta et al and Shilliday et al found that the use of diuretics in critically ill patients with ARF was associated with an increased risk of death and nonrecovery of renal function. If medications are not effective, the choice of treatment and dialytic therapy should ideally mimic the efficacy of the native kidney and, at the same time, not delay the recovery of renal function. Therapy should be individualized according to each patient’s urgency and need for the therapy and hemodynamic tolerance.

Intermittent Hemodialysis
Intermittent hemodialysis is still a commonly used treatment for ARF in the critical care unit for some patients. The dialysis is typically done 3 times a week. This timing evolved to ensure that patients were treated sufficiently to provide an “adequate” state of health. These treatment principles applied to patients in chronic renal failure, not to critically ill patients.

Intermittent hemodialysis is also used for many patients because it is relatively inexpensive (approximately $130 per treatment, not including staffing) and of short duration (typically 3-4 hours). Treatment of a patient 3 times a week allows for a considerable increase in the serum levels of urea nitrogen and creatinine and for variations in electrolyte, water, and acid-base balance between treatments.

Orders for intermittent hemodialysis typically require, at a minimum, removal of the previous 24 hours’ fluid intake during the dialysis treatment. Critically ill patients are prone to hypotension because of the severity of their illness. Therefore, removal of 2 to 3 L/h of fluid in a patient in an unstable condition may make it difficult to use conventional intermittent hemodialysis.

As a result, critically ill patients with ARF will not achieve adequate water or waste removal with traditional dialysis. Repeated episodes of hypotension during intermittent hemodialysis also can lead to ischemia of the nephrons each time the dialysis is performed. Therefore, the ability of the remaining nephrons to survive, as well as the potentially adverse effects of aggressive fluid removal, should direct the choice of therapy. Continuous Renal Replacement Therapy
As the search for better treatments for ARF continues, research findings are indicating that the technique and timing as well as the type of renal replacement therapy used may affect patients’ survival and recovery of renal function. The concerns about hemodynamic stability during hemodialysis, nephron injury, and the inability to adequately remove excess water and solutes have led to the development of a slower, less aggressive renal replacement therapy: continuous renal replacement therapy (CRRT).

CRRT is an extracorporeal process in which blood is removed from the arterial lumen of a catheter by a peristaltic blood pump and pushed through a semipermeable membrane before being pumped back into patients via the venous lumen of the catheter. These catheters are typically placed in the internal jugular or subclavian vein. When the blood passes through the membrane (hemofilter or dialyzer), electrolytes and small- and medium-sized wastes are removed from the blood by convection and diffusion. Fluid removal is achieved by ultrafiltration at an established hourly rate and on a continuous basis.

Types of CRRT
In 1977, Kramer et al described a therapy called continuous arteriovenous hemofiltration in which a patient’s own blood pressure moved the blood from an artery to a vein through a highly porous hemofilter. The blood flow through the hemofilter was driven by the patient’s mean arterial pressure, and ultrafiltration was achieved by raising and lowering the drain bag in relation to the patient. The blood flow rate was slow because of frequent hypotension experienced by critically ill patients. It resulted in a low driving pressure of the blood through the circuit, much less than what a blood pump can achieve. This slow blood flow limited the volume of ultrafilterate that could be obtained, which limited the adequacy of the dialysis. A major drawback to continuous arteriovenous hemofiltration was the use of a large catheter in a major artery, commonly the femoral artery, a practice associated with risks for infection, distal thrombosis formation, disconnection, and exsanguination.

In the 1980s, a blood pump, such as those used in intermittent hemodialysis, and a double-lumen catheter in a large vein were used to provide a consistent blood-flow rate without the risks associated with the arteriovenous approach. This method of CRRT was called venovenous hemofiltration and has been adopted as the standard for CRRT.
CRRT mimics the functions of the kidneys in regulating water, electrolytes, and wastes by continuing 24 hours a day, for several days, slowly removing fluid and solutes. The indications that led to the development of CRRT include patients who had fluid overload, diuretic resistance, hemodynamic instability, and azotemia. Because fluid removal with CRRT is much slower than with intermittent hemodialysis, CRRT is an ideal therapy for critically ill patients in unstable conditions. For example, a net ultrafiltration rate of 12.5 mL/min is required to remove 3 L of plasma water during 4 hours of intermittent hemodialysis. The same amount can be removed with CRRT in 24 hours with a net ultrafiltration rate of 2 mL/min. Removing fluid more slowly and in smaller volumes in hours or days may provide enhanced hemodynamic stability.

Membranes in CRRT

High-efficiency membranes are used in CRRT for maximum water and waste removal. High-efficiency membranes include high-flux dialyzers and hemofilters. The membranes used are synthetic and biocompatible. The capability of dialysis membranes lies in the surface area, membrane thickness, pore size and density, and potential to adsorb proteins. High-efficiency membranes have both high membrane permeabilities and larger pore sizes and therefore are desirable for CRRT. In all methods of CRRT, as blood flows through the hemofilter, plasma water is filtered through the pores in the hemofilter membrane and produces the ultrafiltrate. The ultrafiltrate produced during CRRT is composed primarily of water, electrolytes, wastes, and some dialyzable drugs.

High membrane permeability and large pore size provide excellent clearance of small-molecular-weight solutes and larger substances, up to the maximum pore size. Examples of small-molecular-weight substances (<0.5 kd) are urea, electrolytes, vitamins, and certain medications. Large-molecular-weight substances such as albumin, red and white blood cells, and drugs bound to proteins cannot pass through a hemofilter membrane (typically with a maximum pore size of 50 kd) because of the large size of the substances.

Another potential benefit of the use of high-permeability dialyzers and hemofilters is the ability to remove cytokines, which are middle-molecular-weight substances, or decrease their concentration by adsorption to the membrane. These inflammatory cytokines, such as interleukin-1β, interleukin-6, and interleukin-8, contribute to sepsis and may be altered or removed in CRRT. Although no conclusive data confirm the link between the beneficial clinical effects observed in patients with sepsis who have CRRT, the effect of cytokine removal by adsorption and the preliminary observations of patients’ outcomes are encouraging.

Continuous Venovenous Hemofiltration

Continuous venovenous hemofiltration (CVVH, Figure 1) is defined as “a venovenous technique where the ultrafiltrate produced during membrane transit is replaced in part or completely with appropriate replacement solutions to achieve blood purification and volume control.” In CVVH, convection and ultrafiltration are used to remove waste products. Convection is the movement of solutes under pressure through a membrane along with the movement of water. Convective therapies appear to have advantages over other continuous therapies because of the ability to remove a wider range of solutes with the ultrafiltrate, including some cytokines, a characteristic that may affect patients’ outcomes.
Physiological fluids termed replacement fluid are used to replace the majority of ultrafiltrate removed hourly, in order to prevent instability and to replace electrolyte losses during CVVH. Replacement fluids generally consist of balanced electrolyte solutions that closely resemble the composition of the ultrafiltrate lost minus the wastes. Replacing fluids are infused either into the arterial side of the circuit before the hemofilter, a method called “predilution/prefilter,” or into the venous side of the circuit after the hemofilter, a method called “postdilution/postfilter.” Both methods of fluid replacement achieve the goal of replacing ultrafiltrate volume and electrolytes while removing wastes by convection.

The predilution method of infusing replacement fluid also provides a continuous flush for the hemofilter that dilutes the blood flowing through the filter, a situation that may decrease hemofilter clotting and increase the clearance of solutes. Postdilution infusion of solutions replaces fluid and electrolytes but does not affect clotting in the hemofilter. Increasing the volume of ultrafiltrate produced in CVVH by increasing the infusion of replacement fluid increases clearance of both small- and middle-molecular-weight substances by solute drag.

Currently, no electrolyte solutions have been specifically approved by the Food and Drug Administration for infusion as replacement fluid. Solutions that are used include lactate- or bicarbonate-based or custom pharmacy–mixed fluids. Because of the lack of these approved replacement solutions in volumes greater than 1 L, the cost of mixing custom solutions and the ability to provide large volumes for patients’ treatment, some physicians use purchased custom-compounded pharmacy fluids in large volumes or may use commercial solutions as an off-label prescription.

Continuous Venovenous Hemodialysis

In continuous venovenous hemodialysis (CVVHD, Figure 2), diffusion and ultrafiltration are used to remove waste products. The fluids used are known as dialysate fluids. Dialysate is infused countercurrent to the blood flow, into the outside compartment of the hemofilter to provide a diffusion of wastes from the blood. The dialysate fluid is not infused into the blood as in CVVH, rather it is infused into the outside compartment of the hemofilter or dialyzer. In diffusive therapy, small molecular wastes and electrolytes diffuse from the high concentration in the blood into the sterile dialyzing fluid on the other side of the membrane and are removed in the ultrafiltrate.

Historically, CRRT fluids were run at lower flow rates, approximately 1 L/h, because no research was available that indicated better treatment efficiency with higher rates and because many older machines lacked the option to increase flow rates. When dialysate is run at lower flow rates, such as 10 to 20 mL/min, the dialysate is almost completely saturated with the wastes. However, if the dialysate is run at faster rates, 30 to 60 mL/min, the amount of small molecular waste cleared increases. Diffusion in CVVHD does not affect clearance of larger molecular weight substances. Research indicates that increasing the dialysate rate improves the efficacy of dialysis. Most current CRRT equipment allows fluid rates to be prescribed at the higher rates, often up to 150 to 200 mL/min to improve clearance.

For CVVHD, dialysate solutions are available from a variety of sources. The solutions may be mixed by hospital pharmacies, peritoneal dialysate solutions may be used, or commercial solutions approved by the Food and Drug Administration may be purchased. Disadvantages of relying on hospital pharmacies to mix either
dialysate or replacement solutions include the high cost of labor to produce multiple liters of solutions consistently and safely for ongoing CRRT treatments. Peritoneal dialysate solutions contain large amounts of glucose and are lactate based, making them less suitable for CVVHD. Lactate solutions may worsen metabolic acidosis in patients with metabolic derangements and hepatic failure. Bicarbonate-based solutions are preferred for patients with hepatic failure who cannot metabolize the lactate and are also more physiological than are lactate solutions. Several commercial dialysate solutions in large volumes are currently available, such as PrismaSate (Gambro, Lakewood, Colo), Baxter Premixed Dialysate and ACCUSOL (Baxter, Deerfield, Ill), PureFlow (NxStage Medical, Lawrence Mass), and Duosol (B. Braun, Bethlehem, Pa). These solutions provide a wide choice of electrolyte compositions and the choice of bicarbonate- or lactate-based solutions to meet individual patients’ needs.

Continuous Venovenous Hemodiafiltration

In continuous venovenous hemodiafiltration (CVVHDF, Figure 3), diffusion, convection, and ultrafiltration are used to remove wastes and water. In this method, dialysate and replacement fluids are used simultaneously in various combinations of rates. The goal is to offer both a convective therapy, for clearance of middle-molecular-weight substances, and a diffusive therapy, for removal of smaller substances. This therapy was widely used to provide a more efficient dialysis when machines were limited in the ability to infuse large quantities of fluids. However, current technology for CRRT provides the ability to infuse fluid, either replacement or dialysate, at higher rates to provide efficient therapy. The ability to use only a single fluid effectively also improves the simplicity of performing CRRT.

Slow Continuous Ultrafiltration

Slow continuous ultrafiltration (SCUF, Figure 4) is a hemofiltration therapy used primarily for fluid removal. No dialysate or replacement fluids are used because wastes, electrolyte balance, and acid-base status may not be as critical an issue in patients who have SCUF and in patients who have other CRRTs. As it is removed from the hemofilter, ultrafiltrate is regulated to provide a slow, continuous removal of plasma water for diuresis, for example, 50 to 500 mL/h to achieve fluid balance. SCUF is a good therapy of choice when the only goal is fluid removal and the patient does not have azotemia. Patients who may benefit from SCUF include those who are refractory to diuretics or who need adjunc-
ative fluid removal, such as patients with pulmonary edema, sepsis, heart failure, or acute respiratory distress syndrome who need diuresis to improve pulmonary function. Research indicates that excess fluid that can be effectively and slowly removed in critically ill patients may improve oxygenation, cardiac output, and mean arterial pressure. In infants and children, research suggests that earlier intervention with CRRT and fluid overload is associated with greater survival, indicating that fluid removal may have a beneficial effect on outcome.

**Anticoagulation for CRRT**

During CRRT, a patient’s blood is outside the body and in contact with artificial tubing and filters. The result is stimulation of the coagulation cascade and, more important, the complement cascade if a biocompatible membrane is not used. The goal for anticoagulation in CRRT is to reduce clotting in the hemofilter to maximize the CRRT circuit life. Avoiding interruptions in CRRT by preventing clotting provides continuous therapy for the patient. Although CRRT is intended to run for 24 hours a day, the average therapy time is actually closer to 16 hours a day because of interruptions. These interruptions can decrease the effect and efficacy of CRRT markedly.

CRRT can be performed with or without anticoagulation. The choice of anticoagulant depends on the physician’s preference, the patient’s condition, and the familiarity of the nursing staff with anticoagulation regimens. At times, the choice is to not give a patient an anticoagulant or use an anticoagulant in the CRRT system. Anticoagulation may not be indicated in patients who have recently had surgery, have sepsis or immunosuppression, or have hepatic failure or thrombocytopenia. Another reason to use anticoagulants is to maximize the CRRT circuit life so that the therapy is continuous for several days. This maximization can reduce the cost of the circuit tubing and components, which often cost approximately $150 to $200 or more a set, and thereby reduce the cost of patients’ treatment.

Patients receiving anticoagulation for CRRT should be monitored on a routine basis. The most common tests used to monitor coagulation are activated clotting time and activated partial thromboplastin time (aPTT). Activated clotting times may be maintained at 180 to 220 seconds or according to institutional protocols. The degree of anticoagulation is most commonly determined by using aPTT. The aPTT is maintained at 1.5 to 2 times normal to maintain patency of the circuitry. The bedside nurse is responsible for monitoring any adverse effects of anticoagulation, including hemorrhage, formation of hematomas, thrombocytopenia, and allergic reactions.

Heparin is the most widely used anticoagulant. Other options include citrate, direct thrombin inhibitors, and flushes with isotonic sodium chloride solution. Ideally, anticoagulation is done without producing systemic anticoagulation in the patient. The type of therapy, the anticoagulant used, and the blood-flow rates are all key components of keeping the CRRT system free of clots (Table 1.).

**Table 1 Anticoagulation options in continuous renal replacement therapy**

<table>
<thead>
<tr>
<th>Option</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushes with isotonic sodium chloride solution</td>
<td>Not an anticoagulant, helps flush the hemofilter, possibly prolonging filter life</td>
</tr>
<tr>
<td>Heparin</td>
<td>Easy, inexpensive, may cause bleeding or heparin-induced thrombocytopenia</td>
</tr>
<tr>
<td>Regional citrate</td>
<td>More labor intensive than other options</td>
</tr>
<tr>
<td></td>
<td>Requires diligent monitoring of results of laboratory tests, such as serum levels of sodium, ionized calcium, and bicarbonate</td>
</tr>
<tr>
<td></td>
<td>Requires infusion of calcium outside the circuit</td>
</tr>
<tr>
<td></td>
<td>Provides good anticoagulation</td>
</tr>
<tr>
<td></td>
<td>Large sodium overload occurs when trisodium citrate used</td>
</tr>
<tr>
<td></td>
<td>May cause alkalosis</td>
</tr>
<tr>
<td>No anticoagulation</td>
<td>Variable success</td>
</tr>
<tr>
<td></td>
<td>Need brisk blood-flow rates and may not prevent clotting</td>
</tr>
<tr>
<td></td>
<td>Simplest method</td>
</tr>
<tr>
<td>Regional heparinization</td>
<td>Heparin infused before the filter and protamine infused after the filter</td>
</tr>
<tr>
<td></td>
<td>Requires diligent monitoring of anticoagulation to keep system patent</td>
</tr>
<tr>
<td></td>
<td>Protamine may cause adverse reactions</td>
</tr>
<tr>
<td>Direct thrombin inhibitors (eg, Argatroban, lepirudin)</td>
<td>Good anticoagulation, but much more expensive than other options</td>
</tr>
</tbody>
</table>
Heparin

Heparin is the least expensive anticoagulant and can be used either systemically or regionally. When heparin is used, the hemofilter may be flushed with a dilute heparin solution continuously or intermittently. Systemic heparinization includes infusing heparin into a separate intravenous access or into the arterial side of the CRRT circuit. Infusion of the heparin into the arterial side of the CRRT circuit allows mixing of the heparin with the blood from the patient before the blood reaches the filter (prefilter). The heparin can be infused via an intravenous pump or a syringe pump, depending on the CRRT system used. Systemic heparinization provides anticoagulation of the circuit as well as for the patient.

Heparin-induced thrombocytopenia is a complication of heparin therapy. This complication is well documented and therefore has limited the popularity of heparin for anticoagulation in recent years. Heparin-induced thrombocytopenia occurs when antibodies to heparin bind to coagulation factor IV on platelets, causing platelet activation and aggregation. These changes in turn cause the generation of venous and arterial thrombi and a decrease in the platelet count. Even after heparin is discontinued, the platelet count may remain low. Consequently, in patients with heparin-induced thrombocytopenia, the concerns for thrombi and the associated costs of changing CRRT circuits frequently have led to the use of other anticoagulants in CRRT.

Regional heparinization involves use of an anticoagulant in the circuit only, not systemic heparinization in the patient. Heparin is infused directly via a syringe or an intravenous pump into the circuit blood prefiltter. Protamine, a heparin antagonist, is delivered via an intravenous pump into the circuit near the catheter on the return blood line to deactivate the heparin.

Anticoagulation monitoring for regional heparinization requires determining the aPTT of blood from the patient (eg, blood obtained via a peripheral site or an arterial catheter) and the aPTT of blood in the CRRT circuit (usually from the postfilter preprotamine infusion side of the CRRT circuit) regularly. The goal in regional heparinization is a normal aPTT for the patient and an aPTT of approximately 100 seconds for the postfilter level. Advantages of monitoring of aPTT in both the circuit and the patient include “tight” heparinization, that is, the heparin is not sent to the patient, and therefore anticoagulation occurs only in the circuit. Disadvantages include the requirement for meticulous monitoring of laboratory results and frequent adjustment of dosage of both the heparin and the protamine.

Direct Thrombin Inhibitors

Argatroban (GlaxoSmithKline, Research Triangle Park, NC) and lepirudin (Refldudan, Berlex Pharmaceuticals, Richmond, Calif) are both direct thrombin inhibitors. Direct thrombin inhibitors are used for their anticoagulant properties in patients with heparin-induced thrombocytopenia who are undergoing CRRT and require anticoagulation. Lepirudin is cleared by the kidneys and therefore may not be the drug of choice for patients in ARF. Argatroban is eliminated by the liver and is therefore more suitable for use in patients with renal failure.

Both Argatroban and lepirudin are infused via an intravenous pump into the arterial or access side of the CRRT system. Both drugs are considerably more expensive than heparin.

Citrate

Citrate is also used in CRRT because of the compound’s excellent anticoagulant ability and potential to prolong circuit life. Calcium is an essential component of the clotting cascade. Citrate binds to the calcium in the patient’s blood within the CRRT system and prevents clotting. Citrate is infused prefilter into the CRRT system, and calcium is typically infused via another intravenous line outside the circuit. Ionized calcium levels are routinely monitored because the ionized form of calcium is a the biologically active form of calcium and accounts for about 50% of the calcium in the blood in normal conditions.

Citrate is available as a trisodium citrate or as anticoagulant citrate dextrose formula A. Trisodium citrate has a higher sodium content than does anticoagulant citrate dextrose formula A (420 mmol/L vs 112.9 mmol/L). Citrate is used in CVVH, CVVHD, CVVHDF, and SCUF. Citrate can be used as a replacement fluid that contains less sodium than normal. In CVVHD, a dialysate that also has less sodium than normal may be used to manage the sodium in the citrate solution. Typically, calcium-free solutions are preferred in CRRT to prevent interaction with the infused citrate. Some clinicians use replacement or dialysate solutions containing calcium because the amount of calcium in these solutions...
Flushes With Isotonic Sodium Chloride Solution

When a patient’s condition warrants that no anticoagulant be used, the circuit may be flushed at intervals with small boluses of isotonic sodium chloride solution to reduce stagnation of blood in the hemofilter or dialyzer and keep the circuit free of clots. Some protocols dictate that when no anticoagulant is used, the circuit should be flushed with 50 to 100 mL of isotonic sodium chloride solution each hour to reduce stagnation of the blood in the membrane itself. Isotonic sodium chloride solution is not an anticoagulant, so this maneuver may deter clotting in the hemofilter, but it also increases the volume of fluid intake for the patient.

Maintaining the patency of the CRRT circuit for a patient who is not given an anticoagulant may pose a challenge. Other options to reduce clotting in the circuit include the use of blood tubing that minimizes the air-blood interface, such as eliminating the arterial or venous air traps. Tubing designs that provide methods for air removal without using a large air-blood interface and use of circuit design in which the blood flow moves in straight lines instead of around a blood pump may reduce stagnation and pooling of the blood as the blood flows through the circuit. Because replacement fluid is infused directly into the blood prefilter in CVVH, preventing clotting in the hemofilter by diluting the blood may be helpful. Use of a well-placed, large-bore catheter also can help streamline blood flow from the patient and back to the patient.

Fluid Management in CRRT

Most patients undergoing CRRT are oliguric, anuric, and possibly volume overloaded. The volume of hourly ultrafiltrate removed depends on an hourly fluid-balance calculation and an assessment of the patient’s volume status. Fluid management in CRRT typically involves hourly calculation of the patient’s non-CRRT system intake (eg, infusions, medications, feedings) plus fluid loss ordered by the physician minus non-CRRT system output (eg, urine, drainage fluid, blood loss). Excess fluid volume to be removed in a patient with fluid overload is usually termed “net loss” and is ordered by a physician. An example of net loss volume ordered may be 25 to 200 mL/h more than the hourly intake to ensure a slow and gentle removal of the excess fluid volume (Table 2).

The CRRT system infuses and removes fluid after the fluid balance is calculated and the desired volumes are input to the system. The system monitors the volume of the dialysate and/or replacement fluids infused and the volume of fluid removed on an ongoing basis. Scales or balancing chambers are used to manage the administration and removal of fluid. Any volume of fluid infused outside the CRRT system, such as infusions, tube feedings, boluses, and medications, is not accounted for unless the volume is programmed into the machine to be removed.

If a scale system is used, the scales balance the weight of the volume of fluid programmed to be lost on the infusion scale and the weight gained on the output scale. In a balancing chamber system, the balance chambers empty and fill precisely, to balance the fluid volume programmed.

### Table 2 Typical calculation of fluid balance for continuous renal replacement therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Example, mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: All intake of fluid (eg, infusions, antibiotics, tube feedings, anticoagulants)</td>
<td>80</td>
</tr>
<tr>
<td>B: Desired fluid loss ordered by physician</td>
<td>50</td>
</tr>
<tr>
<td>C: Output in previous hour (eg, chest tubes, drains, nasogastric tubes)</td>
<td>10</td>
</tr>
<tr>
<td>Programmed fluid output</td>
<td>120</td>
</tr>
<tr>
<td>D: Actual fluid volume achieved</td>
<td>110</td>
</tr>
<tr>
<td>Actual net fluid lost: A − C − D</td>
<td>−40</td>
</tr>
</tbody>
</table>
in and out, ensuring that the fluid volume desired is accurate.

In either type of system, to verify accuracy, a nurse can monitor the therapy history, if available, for the volume of actual fluid removed at the end of each hour and compare that volume with the volume that was programmed. The volumes programmed to be infused and removed by the system should be within the manufacturer’s error specifications of the system in use. If the volumes are incorrect, or if the nursing assessment indicates an error, additional troubleshooting is required to achieve the patient’s goals and to ensure the patient’s safety. Every time an alarm occurs, or the pumps stop on the system, the fluid removal is also stopped. Therefore, under certain conditions, the programmed volume of fluid to be removed may not be the volume that was removed that hour. Regardless of the type of system used, the fluid balance should be calculated hourly or according to the institutional standard to monitor the patient’s status and fluid balance.

Before CRRT is started, patients should have a complete nursing assessment (Table 3). The assessment includes evaluation of the fluid status and the volume of fluid the patient is receiving each hour, the patient’s baseline blood pressure, dosages of any vasopressors being administered, weight (“dry” weight before admission and current weight), presence of edema, central venous pressure, pulmonary artery occlusion pressures, cardiac index, and cardiac output if the patient has a pulmonary artery catheter in place. Other helpful measurements include arterial blood gases, arterial oxygen saturation, and mixed venous oxygen saturation. Once CRRT is started, ongoing measurements of these parameters indicate the patient’s tolerance of the procedure as well as any improvement in fluid status.

Decreases in blood pressure, central venous pressure, pulmonary pressures, and weight may indicate that fluid is being lost and the patient is experiencing the benefits of CRRT. A marked decrease in blood pressure, mixed venous oxygen saturation, or arterial oxygen saturation; an increase in edema; or weight gain may indicate that the therapy objectives are not being achieved or that the circuit is not functioning properly. In this instance, a physician should be notified and fluid removal should be decreased or stopped until the patient’s condition becomes more stable. Because one goal of CRRT is to reduce fluid overload, the bedside nurse should discuss the possibility of reducing intake to minimal volumes of fluids if at all possible and concentrating medications and infusions to minimize fluid intake.

Mechanical failures can occur if alarms are ignored or bypassed without determining the cause of the alarms. If scales are not properly calibrated, the volumes of fluid administered and removed may not be the programmed volumes. Bypassing alarms without correcting the cause of the alarm is a safety hazard.

Hypothermia in CRRT

Hypothermia is a complication of CRRT. The typical blood circuit can contain anywhere from 110 mL to 200 mL or more of blood outside the body at any time, a situation that contributes to cooling of the patient. Solutions such as replacement fluid and dialysate are used at room temperature. Infusion rates of 2 to 5 L/h or more provide a more efficient treatment than do slower rates; however, such large volumes of fluid can quickly lower a patient’s temperature if the fluids are not warmed.

Effects of hypothermia include dysfunction of clotting factors and platelets, activation of fibrinolysis, and cardiac dysrhythmias. Some CRRT manufacturers offer a blood warmer for the blood in the circuit, but most systems have some type of plate or convective warmer for warming the therapy fluids.

Before CRRT is started and once it has begun, the patient’s temperature should be routinely monitored and the warmer temperature increased as necessary to keep the patient’s temperature near normal. If increasing the warmer temperature does not correct the hypothermia adequately, or fluid warming options are not available, warming blankets and increases in the room temperature may be used. Nursing tasks include monitoring the patient’s temperature, implementing warming interventions if needed, and monitoring for signs and symptoms of infection (e.g., increased white blood cell counts), because the patient’s temperature is masked by the cooling effect of the circuit.

Air Embolus

Air embolus can occur if a patient receives air in the blood returned. CRRT systems have air detectors built in to detect even microbubbles of air. If the system’s safety mechanisms are bypassed, a patient can receive an air embolus. Alarms can occur if the air is not properly removed from the blood circuit during priming or if a port in the circuit is loose or open. Air also can occur.
<table>
<thead>
<tr>
<th>Assessment</th>
<th>Nursing management</th>
<th>Rationale/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall assessment</td>
<td>Obtain information on the following:</td>
<td>Information obtained about the patient’s medical history and current treatments can provide information about the effect of the therapy Knowledge of the patient’s normal values and current status helps to follow trends, instead of individual values</td>
</tr>
<tr>
<td>Cardiovascular assessment</td>
<td>Determine the following:</td>
<td>The patient’s cardiac status and pulmonary pressures indicate the effect of the fluid removal and the patient’s tolerance of the therapy Too much fluid removed can decrease blood pressure significantly</td>
</tr>
<tr>
<td>Respiratory assessment</td>
<td>Measure or calculate the following:</td>
<td>Respiratory status and parameters can indicate positive effects of the therapy Unwanted changes in arterial blood gases, development of acute respiratory distress syndrome, and increases in pulmonary pressures indicate adverse effects of overhydration</td>
</tr>
<tr>
<td>Gastrointestinal assessment</td>
<td>Assess gastrointestinal function and nutritional status</td>
<td>Adequate nutritional balance is important to promote wound healing and provide proper metabolic function</td>
</tr>
<tr>
<td>Renal/ fluid volume assessment</td>
<td>Assess or determine the following:</td>
<td>Ongoing assessment of fluid balance helps determine the effect of the therapy and the patient’s tolerance of it Prescribed fluid-balance goals should be compared with achieved goals A physician should be notified if fluid goals cannot be achieved because the patient’s condition is unstable.</td>
</tr>
<tr>
<td>Neurological assessment</td>
<td>Assess or obtain the following:</td>
<td>Patients undergoing dialytic therapies can become confused as serum urea nitrogen levels increase or decrease This symptom occurs because during dialysis the osmolality of cerebral spinal fluid decreases more slowly than the osmolality of the blood</td>
</tr>
<tr>
<td>CRRT fluid balance calculations</td>
<td>Calculate fluid balance once an hour or per institutional policy</td>
<td>Fluid gains may be indicated by increases in blood pressure, pulmonary capillary wedge pressure, and central venous pressure and a decrease in arterial oxygen saturation Fluid losses may be indicated by decreases in blood pressure, central venous pressure, and pulmonary capillary wedge pressure Patients’ weight often increases as fluid is gained, and an increase in edema may occur Fluid-balance calculations are a potential source of error in CRRT Incorrect calculations can cause unwanted gain or loss of fluid Some patients do not tolerate prescribed fluid removal A physician should be notified about the effect of the prescribed fluid loss</td>
</tr>
</tbody>
</table>

Continued
Table 3  Continued

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Nursing management</th>
<th>Rationale/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing circuit monitoring</td>
<td>Observe or check for the following hourly: Blood-flow rate Venous or return pressures Arterial or access pressures Filter pressures (if applicable) Balance pressures (if applicable) Effluent pressures Color of the blood in the circuit Presence of air</td>
<td>The documentation in CRRT is not individually in each hourly value, but in the trends Changes in pressures (ie, increases in filter, balance, and effluent pressures) can indicate clotting Pressures can also alert nurses about disconnection or catheter dysfunction Blood-flow rates and fluid rates may have to be adjusted according to prescription The color of the blood can indicate clotting (eg, the blood becomes very dark) Air should be assessed continually</td>
</tr>
<tr>
<td>Body temperature</td>
<td>Assess for hypothermia and hyperthermia Use a warmer for fluid or blood if indicated</td>
<td>The patient’s blood is outside the body in a large circuit Hypothermia is a common complication of CRRT Maintaining body temperature promotes healing and helps maintain normal coagulation and normal laboratory values Colder patients may experience cardiac arrhythmias and are prone to using more energy in addition to increasing cardiac output 67,68</td>
</tr>
<tr>
<td>Dialysis catheter care and patency</td>
<td>Monitor catheter patency before and during CRRT and at disconnection of the CRRT system Monitor access pressures hourly to assess catheter flow and detect access problems Manage catheter dressing changes according to institutional policy</td>
<td>Patency of the catheter can affect the effectiveness of the therapy Patency can be quickly evaluated by flushing 10 mL of isotonic sodium chloride solution into each lumen of the catheter and assessing resistance by quickly pulling back the blood into the syringe (remove anticoagulant first if applicable); blood should quickly and easily fill the syringe Aspiration of air bubbles or a “catch” in aspirating blood into the syringe may indicate a problem with the catheter 69,70</td>
</tr>
<tr>
<td>Monitoring of electrolyte balance and dialysis solutions</td>
<td>Check for the proper solution, dialysate, or replacement fluid and the proper infusion site Be sure laboratory work is done routinely or per institutional protocol to assess the effectiveness of the therapy Check the solutions to make sure they are the correct prescription and are infusing into the correct port on the circuit: dialysate into the dialysate compartment and replacement fluid into the prefilter or postfilter infusion ports into the blood</td>
<td>The type of solution used in CRRT can have a significant effect on a patient’s electrolyte levels Monitoring laboratory values can assist in preventing sudden changes in electrolyte levels and provide for prompt intervention 65,71</td>
</tr>
<tr>
<td>CRRT circuit care and management</td>
<td>Provide proper circuit care and interventions to prevent nosocomial infection</td>
<td>All circuit interventions require using precautions such as gloves, masks, and aseptic or sterile techniques to protect the patient from exposure to infectious agents Patients receiving CRRT have a higher risk of bloodstream infections than other patients do 72</td>
</tr>
<tr>
<td>Alarms</td>
<td>Determine the cause of all alarms</td>
<td>Nurses who provide care for patients receiving CRRT should be able to troubleshoot alarms Overriding alarms without investigating the cause is a safety hazard The alarms should also be distinct and loud enough to be differentiated from other alarms in the room</td>
</tr>
</tbody>
</table>
in the circuit if the access cannot provide the blood flow programmed on the machine. In this situation, the blood pump will run, but a vacuum is created, causing air to move through the circuit. In each of these situations, the nurse caring for the patient is responsible for troubleshooting the system to determine the source of the air or for checking the help screens on the system to determine if therapy can be resumed.

After the system is primed and brought to the bedside and before the connection with the patient is established, the circuit should be checked to ensure that all air has been removed. It is imperative to verify that the arterial or access side of the access tubing is securely connected to the catheter and, even more important, that the venous or return side of the tubing is securely attached to the catheter. If the venous side of the blood tubing is not connected securely to the catheter, an air embolism can occur because the blood will have traveled past the machine’s air detector. Nurses must continually assess the circuit tubing for the presence of air.

Minimizing Blood Loss in CRRT

Minimizing blood loss in patients receiving CRRT is always a priority. Prompt attention to alarms and knowledge of troubleshooting can prevent loss of blood in the circuit. Nurses caring for a patient receiving CRRT should know how to perform an automatic or manual return of the patient’s blood when CRRT is discontinued or the circuit is clotted. As mentioned earlier, some circuits can hold 200 mL or more of blood. Ongoing blood loss due to failure to rinse the blood back to the patient or to an inability to detect signs of clotting in the hemofilter is detrimental to the patient and may affect the patient’s safety. Nurses’ yearly competency testing should include a review of rinsing patients’ blood back in addition to a review of machine alarms.

Transport Procedures

At times, a patient receiving CRRT may need to go out of the critical care unit for a diagnostic procedure or test (eg, computed tomography or angiography). Before the patient leaves the critical care unit, the connection with the CRRT system is discontinued, and the patient’s blood is returned to the patient by flushing the blood back with isotonic sodium chloride solution. The machine is placed in a recirculation mode while the patient is away. When the patient returns to the critical care unit, the system is taken out of recirculation mode, the connection between the patient and the machine is reestablished, and therapy is resumed.

Flushing the patient’s blood back in this situation not only minimizes blood loss but also allows maximum use of the CRRT circuit if the circuit is not clotted.

Institutions should have protocols in place to guide the length of time CRRT can be discontinued while the isotonic sodium chloride solution recirculates. Protocols can be developed by using the manufacturer’s guidelines and recommendations from the infection control service and the blood bank.

Innovative Developments

Timing of therapy, early initiation of renal replacement therapy, and the adequacy of dialysis (eg, “dialysis dose”) may affect patients’ outcomes.74-81 The impact of adequate amount or dose of dialysis in ARF has been long debated. In CRRT, an adequate dose is considered the amount of dialysis, with fluids, based on the patient’s weight required to provide a therapeutic treatment, as opposed to conventional dialysis in which not only the patient’s weight but also the time on dialysis is taken into account.36,79 Some think that the actual dose of dialysis delivered in ARF is low and is strongly affected by the patient’s underlying disease process, hypercatabolic state, hemodynamic instability, and volume overload.1,14,82

The importance of dose of dialysis is being examined in a randomized trial83 by researchers at the Department of Veterans Affairs and the National Institutes of Health. The purpose of the trial is to determine the effect of conventional dialysis dose versus intensive dialysis on patients’ outcomes. The aim is to compare traditional methods of dosing in CRRT and intermittent hemodialysis, as well as in slow extended dialysis.

Other dose-related research suggests that higher blood-flow rates (200-300 mL/min) can enhance clearance in CRRT. These higher blood-flow rates combined with fluid infusion rates determined on the basis of body weight may improve morbidity and mortality and also preserve renal function. Ronco et al14 studied administration of replacement fluid at rates of 20, 35, and 45 mL/kg per hour with use of moderate blood-flow rates in CRRT. In patients given fluids at rates of 20 mL/kg per hour, survival was 41%, whereas in patients...
given fluids at 35 and 45 mL/kg per hour, survival was 57%. In addition, 90% or more of the survivors in the 35 and 45 mL/kg per hour group had full return of renal function. The weight-based fluid doses used in the study were higher than the smaller volumes of fluids thought to be beneficial in the past.

**Slow Extended Daily Dialysis**

A therapy that some think provides the same or similar benefits of 24-hour CRRT is termed slow extended daily dialysis (SLEDD) or “SHIFT” therapy, because the therapy is completed during a single nursing shift. SLEDD is done exactly as CRRT is but is completed in a shorter time, such as 8 to 12 hours instead of 24 hours of continuous treatment. Compared with other methods of CRRT, SLEDD requires higher fluid-flow rates, higher blood-flow rates, and higher hourly volumes of fluid removed to condense the treatment. The shorter duration allows patients to be treated with renal replacement, for example, during the night shift but also be free for tests, rehabilitation, or discontinuation of ventilator support during the day.

Diligent assessment of patients’ hemodynamic stability and fluid-volume status is imperative when SLEDD is used because compared with other CRRT methods, approximately double the amount of fluid may need to be removed in a shorter time. During SLEDD, anticoagulant may not be required because of the shorter treatment time. Some researchers have indicated that SLEDD or SHIFT therapy combines excellent waste removal and supports cardiovascular stability and is still as efficient as a 24-hour CRRT.

**Nonrenal Indications for CRRT**

Novel approaches of using CRRT to treat sepsis have been proposed. A method of high-volume ultrafiltration of 4 to 6 L/h for 6 to 8 hours termed pulse hemofiltration may provide benefits such as elimination of cytokines and middle-molecular-weight substances known to cause sepsis. Researchers continue to examine using continuous hemofiltration to remove inflammatory mediators in patients with sepsis.

Ronco et al suggest that the management of patients with multiorgan dysfunction syndrome should focus not only on renal replacement but also on a multiorgan support therapy. Multiorgan support therapy is based on the principle that all organs share one thing in common: contact with blood. Therefore, blood purification and modulation of the blood composition may have a potential effect on all body organs. On the basis of this principle, CRRT may support several organs at one time by early detection and correction of the abnormalities that occur in multiorgan dysfunction syndrome.

The results of other studies suggest that sepsis can be treated by using hemoperfusion. In hemoperfusion, a plasma filtrate sorbent filter is used in place of a hemofilter on a CRRT-type circuit. In hemoperfusion, adsorption of the solutes is a primary mechanism of cytokine clearance. The sorbent filter used can be either charcoal or a synthetic material. The filters adsorb cytokines and appear to improve survival in animal models of sepsis.

A similar treatment for sepsis is coupled plasma filtration. In this treatment, plasma is filtered to improve blood purification; blood is passed through a hemofilter-type membrane with larger pores so that the blood is separated from the plasma water and proteins, which are removed. The plasma is then pumped through another filter to remove water and smaller molecular weight substances. Because the substances removed are larger than those removed in CRRT alone, the benefit of coupled plasma filtration may be an increase in the removal of cytokines from the plasma of patients who have sepsis. This model is based on the benefits of plasmapheresis in critically ill patients.

Treatment of decompensated heart failure with ultrafiltration has been studied in the past and currently is being examined more closely. Patients who have myocardial dysfunction or congestive heart failure are often refractory to conventional therapy (eg, diuretics and inotropic agents). CRRT for the removal of excess fluid can improve myocardial elasticity and cardiovascular stability and optimize fluid balance for patients who may also have some degree of renal impairment. Some applications of this therapy include the use of traditional CRRT machines to perform SCUF for short periods and the use of more specialized equipment and peripheral intravenous blood access for simple removal of plasma water.

The use of a bioengineered artificial kidney is yet another exciting area of research. Humes et al have performed research in the treatment of patients in ARF in which CRRT is used in tandem with a bioartificial kidney, known as a renal tubule assist device. CRRT can replace some functions of the kidneys, such as water and waste removal,
but it does not provide the metabolic, immunological, or endocrine functions of the kidneys. This bioartificial kidney contains human renal proximal tubule cells that are grown and seeded inside the fibers of a conventional hollow fiber dialyzer. Humes et al postulate that when the tubule cells are bathed in ultrafiltrate from the CRRT circuit, the cells act similar to a human kidney. The use of human renal tubule cells may provide a dynamic, interactive, and individualized therapy that responds to the pathophysiological conditions of critically ill patients, reducing morbidity and mortality by providing a more complete renal replacement therapy.104,105 Phase 2 clinical trials with the bioartificial kidney have recently been completed, and some results are promising.

Studies106,107 to date have indicated that mortality does not differ between patients who have had CRRT and patients who have had intermittent hemodialysis, but critically ill patients may experience other benefits from CRRT that are not possible with intermittent hemodialysis. Although CRRT has many benefits, like any other therapy, it does not guarantee survival. Patients requiring CRRT are often in a tenuous situation, and once CRRT is started, the therapy may or may not be discontinued without resulting in death. The decision to initiate CRRT requires clear and explicit understanding by patients and their families about the therapy and the potential that the therapy may or may not affect recovery. Critical care nurses have a responsibility to advocate for patients and patients’ families, encourage questions, and participate in education of patients and patients’ families about CRRT.

Recent research indicating treatment with larger volumes of fluids each hour to provide a more adequate therapy may affect how CRRT continues to be used in critical care units.84,88-90 Some centers have set standards for care of patients receiving CRRT that require a ratio of 1 nurse to 1 patient, not only because of the severity of illness of patients receiving CRRT but also because of the additional burden of managing multiple liters of fluid volumes each hour and monitoring an extracorporeal blood circuit.5,71 This paradigm shift may contribute to an increased nursing workload if containers of therapy fluid and ultrafiltrate require replacement and disposal several times a shift or per hour. (Note: most commercial fluid and disposal bags are 2.5- to 7-L bags.) If the practice of using higher volumes of fluids increases, the issue of nursing time required to replace multiple liters of fluids for therapy and dispose of larger volumes of ultrafiltrate more frequently will have to be addressed.

Summary

Currently, mortality associated with ARF remains high, and CRRT is becoming the therapy of choice for the treatment of ARF in critically ill patients. CRRT has many benefits for patients in the critical care unit, including improved hemodynamic stability, excellent fluid and solute removal, and possibly other benefits such as enhanced cytokine removal and prevention of sepsis. The use of CRRT in a multicenter trial may be necessary to validate its efficacy in the treatment of ARF. The use of CRRT for nonrenal indications and in conjunction with a bioartificial kidney will require further research and may offer promise for patients in whom ARF develops in the critical care unit.

Financial Disclosures

None reported.

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Learning objectives:
1. Identify indications for intermittent dialysis and continuous renal replacement therapy (CRRT)
2. Review variations and advantages and disadvantages of CRRT
3. Examine potential complications of CRRT

1. What is the mortality rate associated with acute renal failure?
   a. 0% to 15%
   b. 10% to 25%
   c. 25% to 90%
   d. 90% to 100%

2. What type of medication is used to manage acute renal failure?
   a. Loop diuretics
   b. Ace inhibitors
   c. Angiotensin blockers
   d. Beta blockers

3. What is the goal of ideal treatment of acute renal failure?
   a. Return to adequate state of health by periodic removal of wastes and excess fluid
   b. Mimic efficacy of native kidney and not delay recovery of renal function
   c. Return to maximum state of health by removal of previous 24-hour fluid intake
   d. Mimic efficacy of native bladder and urethra and not delay recovery of bladder function

4. How does intermittent dialysis affect the kidney in a critically ill patient?
   a. Potential for ischemia of ureters and bladder-causing spasm
   b. Potential for ischemia of nephrons
   c. Potential for ischemia of abdominal wall
   d. No ischemia since dialysis works effectively to safeguard nephrons

5. How are wastes removed from the blood with CRRT?
   a. Convection and diffusion
   b. Conduction and transfusion
   c. Convection and transfusion
   d. Conduction and diffusion

6. How is fluid removed from the blood with CRRT?
   a. Diuretics
   b. Transfusion
   c. Ultra filtration
   d. Conduction

7. What was a major drawback to continuous arteriovenous hemofiltration?
   a. Use of large catheter in a major artery
   b. Required arteriovenous fistula
   c. Required peritoneal catheter
   d. Required large catheter in major vein

8. What types of substances cannot pass through a hemofilter (max pore size of 50kd)?
   a. Urea
   b. Electrolytes
   c. White blood cells
   d. Vitamins

9. What is a benefit of predilution fluids?
   a. Removes wastes
   b. Provides electrolytes
   c. Provides ultra filtrate volume
   d. Provides continuous flush for hemofilter

10. How does continuous venovenous hemodialysis (CVVHD) differ from continuous venovenous hemofiltration?
    a. Dialysate is infused into blood in CVVHD
    b. Dialysate is infused into the outside compartment of the dialyzer in CVVHD
    c. Blood is infused into dialysate in CVVHD
    d. Blood is infused into the outside compartment of the dialyzer in CVVHD

11. What type of CRRT is best for fluid removal if the patient does not have azotemia?
    a. Continuous venovenous hemodialfiltration
    b. Continuous venovenous hemofiltration dialysis
    c. Continuous venovenous hemofiltration
    d. Slow continuous ultra filtration

12. What is a complication of CRRT?
    a. Gallstones
    b. Gout
    c. Hypoxia
    d. Hypothermia
Continuous Renal Replacement Therapy in the Adult Intensive Care Unit: History and Current Trends
Susan Dirkes and Kimberly Hodge

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