CHAPTER 144

Starting and Stopping Renal Replacement Therapy in the Critically Ill

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OBJECTIVES

This chapter will:

1. Evaluate the factors that determine need for dialytic intervention in critically ill patients and describe the current status of initiation of renal replacement therapy in the intensive care unit (ICU).
2. Define and contrast approaches for renal replacement and renal support in the ICU.
3. Discuss the practical aspects of initiating and withdrawing dialysis in critically ill patients.

PREDICTORS FOR DIALYSIS REQUIREMENT

When renal replacement or renal support is required, there is a far worse prognosis than with lesser degrees of renal injury.[1–3] There is little consensus among nephrologists and intensivists regarding indications for starting renal replacement therapy (RRT) in a specific patient. In a survey by Ricci et al.,[4] 560 attendees of a critical care nephrology conference listed 90 combinations of indications for initiating treatment. Oliguria/anuria was the most frequent choice, at only 27%. This is less surprising when one considers that acute kidney injury (AKI) has multiple causes and clinical manifestations. The unique combination of factors in a particular case should dictate the timing and type of therapy offered. Although the balance between risks and benefits of invasive procedures must be considered carefully in the individual patient, evidence in favor of early intervention has grown steadily. In 1998 Bellomo and Ronco proposed 12 indications for initiating dialysis in critically ill patients.[5] In their schema, combinations of two or more indications make initiation of RRT "urgent and mandatory." The indications for RRT replacement and RRT support are presented in Boxes 144.1 and 144.2.

Hyperkalemia, severe hyperphosphatemia, severe hyperuricemia, severe acidemia, and uremia-related complications (coma, pericarditis, seizures) are accepted indications for starting dialysis. However, there is wide variability regarding the timing of initiation of dialysis, even when these indications are present. Aside from situations in which there are severe derangements, most nephrologists have a tendency to avoid dialysis for as long as possible. Two major factors contribute to the decision to delay dialysis. First, the dialysis procedure is not without risk. Hypotension, arrhythmias, and complications of vascular access placement are not uncommon.[6] Second is the concern that dialysis may delay recovery of renal function.[7,8] Therefore in general, dialysis in current practice is initiated when clinical features of significant volume overload and solute imbalance dictate a need for intervention. Common parameters used to define the indication and timing of dialysis in patients with AKI include the levels of blood urea nitrogen (BUN) and creatinine, presence of oliguria, evidence of heart failure and pulmonary edema, and an estimate of the catabolic state.[9,10]

Neither laboratory nor clinical data alone seem to predict when dialysis should be initiated. The combination provides the basis for the decision-making process in initiating therapy with dialysis. AKI involves a complex physiologic milieu that requires early aggressive collaborative management to provide appropriate therapy in a timely manner. Careful clinical assessment of the patient, review of laboratory parameters for trends, and knowledge of anticipated events are key to the appropriate management of these intensive care unit (ICU) patients. The following parameters should be considered.

BLOOD UREA NITROGEN

BUN generally is considered to be nontoxic, except for its impact on platelet function and, rarely, when initiating dialysis in the face of elevated intracranial pressures. However, many observational and retrospective studies have shown improved survival for patients who start dialysis at lower levels of BUN.[11–13] In one such study among 100 posttraumatic AKI patients, investigators showed higher survival among those who were initiated on dialysis when BUN was less than 60 mg/dL as compared with those who were started on dialysis when BUN exceeded 60 mg/dL (39% vs. 20.3%; $p = .041$).[11] Among the critically ill, a study of 243 patients with AKI, Liu et al.[14] found that 60-day mortality was significantly greater when dialysis was started with BUN levels of at least 76 mg/dL, despite an apparently lower burden of comorbidities than those patients with lower BUN (relative risk [RR] 1.85; 95% CI 1.16–2.96). In contrast, a randomized controlled trial conducted in oliguric critically ill patients in Europe revealed no significant difference in hospital mortality with early (mean BUN, 46 mg/dL) versus late (105 mg/dL) initiation of hemofiltration.[15] These findings have been disputed because they did not account for nonrenal dependent processes that influence BUN. Volume depletion, hyperalimentation, gastrointestinal bleeding, and exogenous glucocorticoids raise BUN and are seen commonly in AKI patients in critical care settings. Further, the low-BUN groups may have included patients who would have improved without dialysis.[16] Similarly, in a multicenter retrospective study among 1847 ICU patients with AKI, no correlation was found between serum urea levels at the time of dialysis and mortality.[17] Recently, in an online survey presented to 172 nephrologists, Thakar et al. showed that proportion of physicians considering early dialysis at a BUN level of 75 mg/dL or less increased from 17% to 30% to 40% with an increased severity of patient illness.[18] In conclusion, BUN concentration is influenced by volume of distribution, production, and catabolic rate and tubular reabsorption, and one should be prudent to consider the level of BUN carefully in the decision to initiate dialysis.[19]

BOX 144.1

Criteria for Initiation of Renal Replacement Therapy in Adult Critically Ill Patients[a]

Commonly Encountered Indications
Volume overload with severe respiratory or cardiac manifestations
Oliguria or anuria
Output <400 mL/day
Output less than obligatory input
Hyperkalemia with $[K^+] > 6.5$
Acidemia with pH < 7.1–7.2
Azotemia with BUN > 76–100[†]
Creatinine clearance <10 mL/min[b]
AKI after cardiac surgery

Less Commonly Encountered Indications
Poisoning or drug overdose with dialyzable toxin
Uremic encephalopathy and neuropathy
Uremic platelet dysfunction

AKI, Acute kidney injury; *BUN,* blood urea nitrogen.
[a]The presence of any one of these indications may be sufficient to initiate RRT. The presence of two or more makes RRT urgent. Combined derangements should lead to initiation of therapy before the suggested limits have been reached.
[b]When prolonged for 1–2 days without evidence of renal recovery.
Modified from Bellomo R, Ronco CS. Indications and criteria for initiating renal replacement therapy in the intensive care unit. *Kidney Int.* 1998;66(Suppl):S106–S109.

BOX 144.2

KDIGO Recommendations for Initiation of Renal Replacement Therapy in Adult Critically Ill Patients[89]

5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist. (Not Graded)
5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (Not Graded)

Renal Replacement
Life-threatening indications
- Hyperkalemia
- Acidemia
- Pulmonary edema
- Uremic complications (pericarditis, bleeding, etc.)

Nonemergent indications
- Solute control (BUN, SCr)
- Fluid removal
- Correction of acid-base and electrolytes

Renal Support
Volume control
Drug delivery
Nutrition
Solute modulation

From KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012;2(1):1–138.

CREATININE AND CREATININE CLEARANCE

Many studies have demonstrated that serum creatinine (SCr) alone is a suboptimal indicator of renal function during AKI. Use of creatinine as a marker is confounded by age, muscle mass, hydration status, assay interference, and certain medications. Several studies have shown that AKI survivors tend to have higher SCr levels than nonsurvivors.[20–22] The plausible explanation for these observations may be attributed to low muscle mass and volume overload, contributing to lower SCr level and in reality reflecting overall poor health status. Rhabdomyolysis may be an exception because SCr appears to correlate with AKI and the eventual need for RRT in these patients.[23] In actual practice, clinicians often are confronted with a patient whose AKI is manifested only by increases of BUN and creatinine. In an international practice survey, 43% to 60% of nephrologists choose absolute SCr levels exceeding 5 mg/dL to be a more influential factor than relative increment of SCr to initiate dialysis.[18] However, the literature supporting the role of SCr as a trigger for dialysis is inconclusive. In retrospective study of 98 patients with AKI post–abdominal surgery, Shiao et al. have shown survival benefit for patients who were started on dialysis at RIFLE stage Risk as compared with RIFLE Injury (RR 2.1; 95% CI 0.9–4.9) or RIFLE Failure (RR 3.2; 95% CI 1.3–8.1),[24] whereas other investigators have shown no differences in hospital mortality among patients who were started on dialysis at RIFLE Risk or RIFLE Injury/Failure.[25] The creatinine clearance may be calculated from a timed urine collection over 1 to 24 hours. The longer the time for collection, the higher is the likelihood for errors caused by inaccurate recording of time and incomplete urine collection. Several studies have shown that short-duration (1 to 4 hours) creatinine measures are feasible in the critically ill, and studies have validated the method comparing to 24-hr clearance. The average of SCr values obtained at the beginning and at the end of the collection should be used in the clearance calculations to account for the dynamic nature of AKI.[26]

URINE OUTPUT

Oliguria and its associated complications are serious contributors to morbidity in AKI. Recent study by Kellum et al. has shown that patients who meet oliguric AKI criteria have a worse prognosis than those with nonoliguric AKI.[27] Daily urine output of less than 400 mL that does not improve with diuretics in a patient who is volume replete typically is cited as an indication for RRT.[28] In two cardiac surgery studies, early initiation of dialysis based on urine output below 100 mL during the first 8 hours after bypass surgery showed better survival.[29,30] Higher thresholds should be considered for the patient with significant obligate inputs, such as blood products, antibiotics, and nutritional support. Trends in output should be respected, regardless of the current hourly flow. The combination of fluid overload and low urine output probably may guide toward initiation of therapy. Decreasing output in the face of evolving sepsis is tolerated poorly and is unlikely to respond to diuretics. Anuria is indicative of a severe kidney injury. It rarely improves quickly enough to forestall the need for dialysis in the absence of volume depletion. The use of diuretics to support urine flow has been debated in the literature with no clear indication that it either hurts or helps in oliguria.[31–34] Diuretics generally are ineffective without at least some preexisting urine flow. Given the added comfort of volume control, maintenance of urine volume with or without diuretics may delay unnecessarily the onset of dialysis in select individuals. Liangos et al. examined the relationship of urine volume to timing of initiation of dialysis and overall mortality.[35] Nonsurvivors had significantly higher urine volumes and severity of illness than survivors (1.5 vs. 0.7 L/day). Nonsurvivors also had lower BUN values at

the start of the nephrology consultation (42 vs. 76 mg/dL; $p = .01$).[35] What this study demonstrated was the increasing complexity of the natural history of AKI. Seemingly mild clinical deterioration (as evidenced by a lower Acute Physiology and Chronic Health Evaluation [APACHE II] core at consultation) resulted in delayed initiation of therapy and, ultimately, poor outcomes.

FLUID BALANCE

Volume overload is often the immediate indication for starting RRT. Several pieces of evidence point to the importance of fluid overload in determining outcomes from AKI.[36–43] In a study of 618 critically ill patients, Bouchard et al. showed fluid overload (i.e., percentage fluid accumulation >10%) to be associated independently with mortality (adjusted odds ratio = 2.07).[37] Similarly, in a subgroup analysis of the multicenter Sepsis Occurrence in Acutely Ill Patients (SOAP) study, Payen et al. showed an inverse relationship between fluid accumulation and survival among 1120 patients with sepsis-related AKI.[38] In the RENAL multicenter ICU study among 1453 patients, a negative mean daily fluid balance was associated consistently with improved clinical outcomes.[43] We showed in a randomized controlled trial comparing intermittent therapies to continuous therapies that patients dialyzed for solute control had a better outcome than those dialyzed for volume control.[44] Moreover, patients dialyzed for solute and volume control had the worst outcome. Mukau and Latimer showed that 95% of their patients with postoperative acute renal failure had fluid excesses of more than 10 L at initiation of dialysis.[45] Recent studies suggested that achieving a negative fluid balance within the first 3 days after admission for septic shock was a predictor of better survival.[46] Foland et al. showed that pediatric patients receiving continuous venovenous hemodialysis (CVVH) who have greater than 10% fluid overload before initiation of CVVH have a poor prognosis.[47] Consequently, fluid regulation seems to be an important consideration when deciding to initiate dialysis in the ICU patient with acute renal failure. Moreover, such renal support provides volume "space," which permits the administration of nutritional support without limitations.[48] Generally, RRT is considered preferable to intubation and mechanical ventilation. Conservative strategies involve minimizing inputs, increasing oxygen delivery, maximizing diuretics, controlling the heart rate, and employing vasodilators. When those options fail to maintain the oxygen saturation at 90% or higher, extracorporeal volume removal becomes necessary. If placement of a temporary dialysis catheter is delayed until oxygen saturation reaches this threshold, the patient may not tolerate lying supine for the procedure. Therefore the clinician should consider the patient's ability to lie flat long enough for catheter placement in determining when to start RRT.

HYPERKALEMIA

There is no universally accepted serum potassium level for initiation of RRT. However, a value greater than 6.5 mEq/L should prompt consideration of dialysis. In many cases, hyperkalemia can be treated conservatively.[49–51] RRT becomes more urgent under the following conditions:

1. The potassium concentration is too high to be lowered rapidly into a safe range by shifting it into the intracellular space. Administration of insulin and glucose or high-dose β-adrenergic therapy can each lower potassium by up to 1 mEq/L. The effects of bicarbonate therapy are less predictable.
2. The electrocardiogram (ECG) demonstrates changes typical of serious hyperkalemia. The absence of ECG changes should not be the sole criterion for delaying dialysis, however, because the changes can evolve rapidly to asystole.
3. There is ongoing addition of potassium to the extracellular fluid. Typical cases would involve massive cell lysis, as can be observed in hepatic necrosis, rhabdomyolysis, and some myeloproliferative disorders.
4. There is a concomitant acidosis or beta blockade. Both can inhibit the passage of potassium into the intercellular fluid, minimizing the ability to compensate for a potassium load.
5. There is a loss of ability to remove potassium from the body with potassium-exchange resins. These are active in the colon. It is important to determine whether the colon has been removed or whether the patient has intestinal obstruction or ileus before using this method.

ACIDOSIS

Acidosis is associated variably with ICU mortality, depending on the underlying disease process and available compensatory mechanisms. Severe acidemia contributes to hypotension (by multiple mechanisms), hyperkalemia, hyperventilation, and respiratory fatigue. A pH of 7.20 is a reasonable therapeutic target for avoiding these and other complications.[52] Inability to achieve pH 7.20 with conservative measures such as exogenous bicarbonate replacement and hyperventilation should prompt initiation of RRT. Respiratory acidosis appears to be better tolerated than a metabolic acid load, although there is evidence that uncompensated acidosis is a risk factor for mortality in chronic obstructive pulmonary disease[53] and status asthmaticus.[54]

PLATELET DYSFUNCTION

Uremic patients have a bleeding tendency resulting from multifactorial platelet dysfunction that correlates with the bleeding time. Although there is considerable debate about the clinical utility of bleeding time in the individual patient, the bleeding tendency has been well documented, starting at relatively modest degrees of kidney failure. For instance, Anderson et al. demonstrated a significant increase in bleeding complications and the need for blood product transfusions in cardiac surgery patients with creatinine concentrations higher than 1.5 mg/dL.[55] Using the same cutoff points, O'Brien et al. similarly found excess bleeding risk in general surgery patients.[56] In the ICU, this is clinically important when dealing with gastrointestinal and intracranial hemorrhage or when contemplating invasive procedures. The initial step in management should be to increase the hematocrit to 30%, to improve red cell rheology. The specific platelet defects can be addressed by administering desmopressin (DDAVP) to increase levels of preformed von Willebrand factor, transfusing cryoprecipitate, and, if sufficient time is available, administering conjugated estrogens. Should these be ineffective, dialysis may improve the bleeding time substantially, although there are few available outcome data to support the institution

of RRT.[57,58] Heparin- free hemodialysis should be preferred in patients with active bleeding. It is unclear if peritoneal dialysis has an advantage over hemodialysis for the treatment of uremic bleeding.[59]

UREMIC ENCEPHALOPATHY AND NEUROPATHY

Acute uremia can contribute to alterations of mental status or clouding of consciousness in critically ill patients.[60,61] Uremic encephalopathy is rarely clinically significant in the absence of a separate central nervous system process, such as posterior reversible encephalopathy, stroke, hypercalcemia, or hepatic failure. Acute uremic encephalopathy is reversible with dialysis with time lag of 1 to 2 days. Similarly, acute uremic peripheral neuropathy usually is an exacerbation of a preexisting process such as diabetic neuropathy. Patients with these conditions may improve with institution of dialysis, sometimes dramatically. However, in most cases, institution of dialysis will not provide a substantial benefit unless the underlying processes also are addressed. The nephrologist may be asked to provide RRT to an encephalopathic patient near death, either to ascertain the patient's wishes or to permit a family to say farewell. Dialytic intervention in such hopeless cases probably should be considered futile therapy.

RENAL REPLACEMENT THERAPY FOR MULTISYSTEM ORGAN FAILURE

The effects of CRRT on modulating the levels of inflammatory mediators have been proposed to improve patient outcomes independently of kidney function. Several studies in patients with multiple organ dysfunction syndrome (MODS) have tested different techniques: high volume hemofiltration, high adsorption hemofiltration, high cutoff membranes, and hybrid systems such as coupled plasma filtration absorbance. Experimental and small human clinical studies have suggested that high-volume hemofiltration (HVHF) may improve hemodynamic profile and mortality; however, larger trials failed to confirmed this effect. In the IVOIRE trial,[62] HVHF at 70 mL/kg/hr showed no benefit on mortality, early improvements in hemodynamic profile, or organ function as compared with contemporary standard volume HF (SVHF) at 35 mL/kg/hr. In a systematic review and meta-analysis, there was no difference in 28-day mortality or recovery of kidney function, lengths of ICU and hospital stays, vasopressor dose reduction, and adverse events using HVHF for septic AKI.[63]

Pilot trials in septic patients using high-permeability hemofilters, with increased pore size, which facilitates the filtration of inflammatory mediators, have demonstrated positive immunomodulation, altering neutrophil phagocytosis as well as mononuclear cell function ex vivo. Specific clinical situations can benefit more clearly from early initiation. Removal of lithium and ethylene glycol, for example, are associated with improved outcomes when early therapy is initiated. Super high-flux membranes with larger pore sizes offer significantly greater myoglobin removal and may improve AKI because of massive rhabdomyolysis. In an experimental study,[64] extended dialysis with a high-flux, high-permeability membrane allowed effective elimination of myoglobin with a clearance of myoglobin that surpassed all previously reported dialysis techniques. Although some series of patients have demonstrated that this membrane may be advantageous in preventing AKI or avoiding complete loss of kidney function in patients with rhabdomyolysis,[65] further studies are needed to determine whether improving renal recovery or mortality in patients with AKI resulting from rhabdomyolysis is possible.

In acute myeloma, high cutoff (HCO) membranes are more efficient at clearing free light chains as compared with plasma exchange. Some case reports have suggested a benefit to early use of HCO-HD in cases of cast nephropathy. Hutchison et al.[66] demonstrated an early reduction in free light chains to be associated with renal recovery. The same group demonstrated a high rate of independence of dialysis in AKI patients with cast nephropathy who received HCO-HD.[67] Although the evidence for the indication is still being developed, there is hope that HCO-HD may improve kidney outcome in myeloma patients.

RENAL SUPPORT VERSUS RENAL REPLACEMENT

In spite of the absence of standards for initiation of dialysis in the ICU, several important factors must be considered when making the decision to provide RRT. An important distinction in the ICU patient is the recognition that acute renal failure does not occur in isolation from other organ system dysfunction. Consequently, providing dialysis can be viewed as a form of *renal support* rather than mere replacement.[68] For example, in the presence of oliguric renal failure, administration of large volumes of fluid to patients with multiple organ failure may lead to impaired oxygenation. In such a setting, early intervention with extracorporeal therapies for management of fluid balance may affect significantly the function of other organs irrespective of more traditional indices of renal failure, such as BUN. This terminology distinguishes between the strategy of replacing individual organ function and one of providing support for all organs. Continuous RRTs are suited particularly to provide renal support in the ICU patient. The freedom to provide continuous fluid management permits the application of unlimited nutrition, adjustments in hemodynamic parameters, and achievement of steady-state solute control, which is difficult with intermittent therapies. It is thus possible to widen the indications for renal intervention and provide a customized approach for the management of each patient.

The benefits of supporting other organs depend on the balance between the burden imposed by clinical conditions and the current ability of the kidneys to manage fluid and the metabolic load. The imbalance between other organs demands and kidney function leads to unmet needs, which may be ameliorated by additional renal support. Some key factors contribute to demand on renal function and determine renal excretory capacity. When there is an increased fluid accumulation, high catabolic rate, and severe underlying disease, renal function is stressed to the maximum and requires addition of RRT capacity. In a less severe scenario with lower fluid accumulation, normal catabolic rate, and in a less severely ill patient, a level of compromised renal function may be able to meet the needs of other organs. Time of initiation thus should include the consideration of these changing needs, and ideally, RRT should be implemented in anticipation of deterioration of overall organ function.

TIMING OF INITIATION

Some studies have suggested that "early" RRT could improve outcomes in AKI. However, the benefits of RRT must be weighed against its inherent risks. A major issue to further advance in this question is that we have yet to define what constitutes early versus late, and therapeutic interventions are not uniform after RRT initiation. The parameters used to access kidney function are not sensitive nor specific and do not constitute reliable markers on which to base intervention. Nevertheless, the optimal timing of RRT initiation has been the focus of several studies, and current evidence suggests reduced mortality and better renal recovery with earlier RRT initiation.[69]

A recently published pilot multicenter randomized trial investigated the optimal timing of initiation of RRT in critically ill patients with AKI.[70] In a 12-center open-label pilot trial of critically ill adults, they randomized patients to accelerated (12 hr or less from eligibility) or standard RRT initiation. In the accelerated arm, patients started RRT within 12 hours, whereas in the standard arm, the median time to start was 31.6 hours from eligibility. Of patients randomized to the standard arm, 19 did not receive RRT (6 died and 13 recovered kidney function). Mortality was 38% in the accelerated and 37% in the standard arm. In a single-center study, the ELAIN trial, Zarbock[71] et al. examined the effect of early versus delayed initiation in 231 patients who had reached stage 2 AKI per KDIGO guidelines and had severe sepsis, use of vasopressors or catecholamines, refractory fluid overload, or development or progression of organ dysfunction (nonkidney). Early initiation of RRT significantly reduced 90-day mortality as compared with delayed initiation of RRT. In addition, more patients in the early group recovered renal function by day 90 and had shorter duration of RRT and length of hospital stay. Discordant results came from a concurrent study, the AKIKI trial,[72] involving 620 patients with KDIGO stage 3 who required mechanical ventilation, vasopressor therapy, or both but did not have life-threatening complications requiring immediate RRT. Patients were assigned randomly to either immediate RRT or a delayed strategy in which therapy was initiated if patients developed severe hyperkalemia, uremia, metabolic acidosis, pulmonary edema, or severe oliguria for more than 72 hours. Almost half of the patients (49%) in the delayed-strategy group did not receive RRT, and the mortality rate at day 60 did not differ significantly between the early and delayed strategies. In addition, diuresis occurred earlier in the delayed-strategy group. The contradictory results of these trials are partially the result of their different populations; AKIKI was primarily medical patients with sepsis, whereas the ELAIN included surgical patients with higher SOFA scores. In addition, the ELAIN trial used mostly KDIGO stage 3 or metabolic derangement as the indication for RRT, and the AKIKI trial used metabolic derangement only.

In a recent meta-analysis,[73] the impact of "early" versus "late" RRT was evaluated in the last 36 studies (7 randomized controlled trials, 10 prospective cohorts, and 19 retrospective cohorts). No survival advantage was found with "early" RRT among high-quality studies and a subgroup analysis by reason for ICU admission, surgical versus medical, or definition of "early," time versus biochemical, showed no evidence of survival advantage. Among the high-quality studies, there were no significant differences in ICU or hospital LOS. However, we must consider some inherent difficulty in these studies. On one hand, the inclusion of patients with mild AKI who may not require RRT at all likely bias the results favorably toward early intervention. However, although the potential benefits of accelerated RRT include improved solute and electrolyte control, a more conservative approach may benefit patients by avoiding inappropriate therapy in those who would survive without it. Another main concern derives from experimental evidence that recovery from AKI may be delayed or impaired by decreased renal blood flow during RRT.[74] In animals submitted to ischemic AKI, RRT with or without systemic hypotension produced renal injury consistent with fresh ischemia. This finding has been accepted with intermittent HD but appears less likely to occur with CRRT.[75–77]

In the absence of convincing evidence for early initiation of RRT, the tendency is still to avoid RRT as long as possible. A more individualized approach for each patient would be better, weighing the risks of the procedure and the likelihood for renal recovery against the benefits of supporting the kidney and other organs to enhance renal recovery. A timely intervention would provide optimal opportunity for patient improvement and recovery from the underlying illness.

SCORING SYSTEMS TO GUIDE RENAL REPLACEMENT THERAPY

Although the RIFLE criteria were developed and validated for AKI diagnosis and evaluation of severity and not as a parameter to guide RRT initiation, some observational studies have investigated whether initiating RRT in less severe renal injury (i.e., RIFLE classification -0 or R) can be associated with a better survival rate. Previous single-center studies[78] have shown the improved prediction of need for RRT based on cystatin C as a functional marker of AKI in comparison to the performance of the Liano score.[7] In addition, RIFLE staging has been proposed as a criterion for starting RRT with a shift in RIFLE class Injury to Failure. Although one study that analyzed AKI after major abdominal surgery demonstrated benefits,[80] two other studies evaluating mainly patients with sepsis demonstrated similar outcomes with either early or late RRT.[81,82]

There are two major problems with using these definitions. Patients at less severe AKI stages initiating RRT may have severe metabolic disorders in spite of limited renal injury, or even no AKI. In addition, when using RIFLE/AKIN criteria, patients with CKD must have significant metabolic disorders to require RRT before classification with the maximum severity grade, in contrast to patients with previous normal previous renal function. Leite et al.[83] applied SCr and UO criteria and used a time-based approach from AKIN stage 3 by urine output (UO) or SCr to RRT initiation. They were able to demonstrate a reduced mortality rate and reduced need for mechanical ventilation among critically ill AKI patients receiving RRT in the first 24 hours after diagnosis of AKI stage 3.

DISCONTINUING RENAL REPLACEMENT THERAPY

There is very little literature to guide the decision to discontinue RRT in patients recovering from AKI. The underlying insult must have resolved, the patient must have enough urine output to avoid volume overload, and RRT usually is continued until the patient manifests evidence of recovery

of kidney function. In oliguric patients, recovery of kidney function also may be manifest by a progressive decline in SCr concentration after initial attainment of stable values. More objective assessment kidney function recovery can be obtained by measurement of creatinine clearance (CrCl), which should be greater than 10 to 12 mL/min. However, a precise level of kidney function needed to allow discontinuation of renal support has not been established; however, a CrCl less than 12 mL/min is probably inadequate to allow discontinuation of therapy. In the ATN study, renal support was discontinued when the measured CrCl exceeded 20 mL/min and was left to the discretion of providers when in the range of 12 to 20 mL/min.[84] In addition, the patient must be able to receive sufficient nutrition. Ideally, a patient undergoing RRT would continue to receive that therapy until sufficient function is regained. Care should be taken to avoid further injury to the recovering kidney. The treatments should be spaced closely enough to avoid possible deleterious hemodynamic consequences of excessive ultrafiltration.[85] The intervals can be extended as urine output and laboratory indices permit, until it is clear that the patient will not need further therapy.

WITHHOLDING AND WITHDRAWING THERAPY

Nephrologists or intensivists often are faced with decisions regarding the use of dialysis as a life-sustaining therapy. Several factors may influence the decision to offer or withhold dialysis support for critically ill patients. In these situations, it is also common to have a lack of agreement among caregivers and family members on the best course of action. For some patients and family members, dialysis remains an extraordinary therapy that can be declined or delayed for personal or financial reasons. It is not unusual for a patient or family to stipulate that dialysis should not be initiated under any circumstances or not unless the patient's life is threatened directly and immediately by kidney failure. It is prudent to communicate early and regularly with the patient and family members to ascertain their desires, to gauge their level of understanding, and to provide focused education to assist their decision making.

In the case of patients who cannot make their own decisions, the ICU medical decision making should be shared with families or surrogates. Communication is essential and discussion about a patient prognosis and outcomes should be made soon after admission. A multicenter, prospective cohort study has shown that often deaths in intensive care units occurred in incapacitated patients who lacked a surrogate decision maker and an advance directive.[86] In these situations, life-support decisions were made in a manner inconsistent with the American College of Physicians guidelines for judicial review, and most life-support decisions were made by physicians without institutional or judicial review.

In some instances, a time-limited trial should be considered for patients requiring RRT but who have an uncertain prognosis or for whom a consensus cannot be reached about providing dialysis. The time-limited trial also could be applied for continuing therapy before withdrawing dialysis if improvement does not occur. The decision making during time-limited trials should be an ongoing process, during which goals of treatment, clinical outcomes, and duration of the dialysis trial can be reassessed daily.

CONCLUSION

The wide variation in RRT use contributes to a lack of consensus on what parameters should guide the decision to start RRT. To develop a criterion for initiating RRT, it is necessary to determine the various factors that clinicians currently use for deciding to start and stop RRT. We believe that to demonstrate the effect of timing of RRT in AKI critically ill patients, the first necessary step is to create the tools to compare patients with similar clinical conditions and kidney ability to manage fluid and the metabolic load. In critically ill patients, the underlying severity of illness and resulting alterations in organ function create a metabolic and volume demand on renal function. AKI reduces renal excretory capacity, and at any given point in time, the renal excretory capacity may be unable to meet the demand, resulting in a mismatch. The extent of mismatch contributes to the need for additional renal support.[87,88]

Key Points

1. Traditional blood and urinary indicators of AKI including novel serum biomarkers are relatively insensitive indicators to guide initiation of renal replacement therapy.
2. Recently concluded large prospective trials have shown conflicting results on the benefit of early initiation of dialysis.
3. The consideration of timing of renal replacement therapy should involve individual patient characteristics, process-of-care elements, and logistics to achieve therapeutic goals.
4. Approaches to discontinuation of renal replacement therapy are entirely empiric at this point.
5. Dialysis decisions for critically ill patients should be collaborative and involve discussions with family members and the caregiver team. A "trial of therapy" concept should be considered for patients with potentially irreversible organ dysfunction.

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