CHAPTER 93

Renal Replacement Therapy for Septic Acute Kidney Injury

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OBJECTIVES

This chapter will:

1. Highlight the very high mortality rates of patients who receive renal replacement therapy for septic acute kidney injury.
2. Appraise renal replacement modes, clearance techniques, doses, and optimal time to commence treatment in septic acute kidney injury.

Epidemiologic studies conducted across multiple hospitals in numerous countries have identified that depending on case mix, 30% to 60% of patients in an intensive care unit (ICU) have or develop acute kidney injury (AKI), and that this most commonly occurs in conjunction with sepsis.[1–3] When AKI is severe enough to lead to marked metabolic or fluid derangements, renal replacement therapies (RRTs) are considered. Application of these renal supports has increased from 4% to 14% of ICU patients over the last decade, representing either a greater prevalence of severe AKI, a lower threshold for using this therapy, or both.[2]

Despite provision of extracorporeal renal supports, mortality rates remain remarkably high, with 50% to 60% of ICU patients receiving RRT not surviving their hospital admission.[1] Outcomes appear even worse for those with septic AKI. The Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) study, conducted in 23 countries, compared groups of patients with septic AKI and nonseptic AKI who received RRT. Septic AKI patients had a longer hospital length of stay and higher in-hospital mortality rate (70% vs. 52%), which remained significant after adjusting for covariates (OR 1.48; 95% CI 1.17–1.89).[3] Fortunately, about 90% of septic AKI survivors recover renal function and do not require long-term dialysis.[1,4]

Given the prevalence of septic AKI, the increasing use of RRT and the marked mortality rates when this therapy is used, it is crucial to consider how these renal supports are best applied. Until recently, our knowledge about RRT in septic AKI was derived largely from uncontrolled observational reports. Now with increasing implementation of RRT, a number of large-scale controlled clinical studies have been conducted. Although these studies have been undertaken in a heterogeneous group of ICU patients with severe AKI, the largest group of patients enrolled have had sepsis. This chapter discusses the evidence on how we best apply RRT, emphasizing the data available for the group of patients with septic AKI.

MODE OF RENAL REPLACEMENT THERAPY

Dialysis circuits used for patients with chronic renal failure have been the basis of RRT modalities available in the ICU. Modifications have included dialysis using a lower blood flow (e.g., 100 mL/min), premixed bags of sterile dialysis solution, incorporation of hemofiltration, and hardware (machines and circuits) suitable for use in an ICU.

The "mode of RRT" typically has been categorized according to (1) its duration and (2) clearance techniques. Intermittent RRT (iRRT) is applied for less than 12 hours per session, whereas continuous RRT (CRRT) is prescribed with the intention to run for 24 hours per day. Within each

of these "duration modes," a combination of "clearance modes," comprising dialysis, filtration, or a variable combination of both, is applied. Therefore a range of RRT modes are available, and trying to determine the most efficacious mode(s) has been difficult.

Intermittent or Continuous Modes

Whether RRT therapies are best applied as an intermittent or continuous mode to patients with septic AKI has been the matter of long-standing debate. iRRT techniques typically rely on larger extracorporeal blood flows and lead to more rapid correction of metabolic derangements. This mode uses dialysate and replacement fluid sourced from plumbed water with electrolyte solution added. However, iRRT may be poorly tolerated in hemodynamically unstable septic patients and in those who require slower restoration of metabolic equilibrium (e.g., cerebral edema). In the international BEST Kidney study, hypotension was reported more than twice as often during iRRT compared with CRRT, despite CRRT patients having a higher severity of illness.[3]

In contrast, continuous RRT can be performed with lower blood flows and titrated to the patient's hemodynamic status. As patients with septic AKI often are receiving infusion of catecholamines to support mean arterial pressure, CRRT commonly is favored in these circumstances. Continuous RRT also provides more gradual correction of metabolic derangements. However, lower blood flows with CRRT may necessitate increased need for anticoagulation, which may provoke bleeding complications. Longer duration on an extracorporeal circuit also may limit mobility of the patient, may lead to greater clearance of medications and micronutrients, and costs more than intermittent RRT.[5]

Multinational epidemiologic studies of ICU patients receiving RRT for AKI, of whom 41% to 48% had septic shock, reported that CRRT was used for 75% to 80%, iRRT for 17% to 25%, and peritoneal dialysis with slow continuous ultrafiltration in 1% to 3%.[1,2,6] Although continuous modes appear to be most commonly applied to patients with severe septic AKI, there is strong preference for iRRT in some centers. For example, in the recent AKIKI trial investigating timing of RRT initiation in French ICUs, iRRT was the mode chosen for 50% of the patients, despite most having sepsis and 85% receiving catecholamines.[7]

Evidence supporting the optimal "duration mode" of RRT is limited. Most studies comparing outcomes after intermittent and continuous modes have been observational, with varying forms of AKI, different severity of illness, excluded hemodynamically unstable patients, have had small cohort sizes, and have not considered cointerventions. Furthermore, other RRT variables, such as clearance mode, choice of dialysis/replacement fluids, anticoagulation, time to initiation, and type of filter membrane, have not been controlled.

Over the past decade controlled studies have examined the duration mode of RRT.[8–11] A series of meta-analyses that incorporated the accumulating evidence have derived the same conclusion, that there is no apparent mortality benefit (overall 50% to 70%), no difference in hemodynamic instability requiring treatment, no difference in hospital length of stay, recovery of renal function, or need for chronic dialysis.[5,12–14] These conclusions remained after adjusting for confounders and when analyzing just the subgroup of patients with septic AKI.

Since these meta-analyses, there has been a further randomized controlled trial that stratified patients to receive either iRRT (daily for 4 to 6 hours) or CRRT.[15] This study enrolled 316 patients and revealed no difference in mortality, hospital length of stay, or renal recovery. Again, these outcomes were no different when analyzing the subgroup of patients with septic AKI.

Dialysis or Hemofiltration Modes

It remains unclear whether RRT is best delivered as dialysis, filtration, or a combination of both. Removal of low-molecular-weight solutes is similar with both clearance modalities, whereas larger molecules are cleared more effectively with convective therapies.

Cytokines, eicosanoids, endotoxins, and other inflammatory mediators are water soluble, largely unbound in the circulation, and normally eliminated by the kidney. Ultrafiltration has been shown to enhance clearance of inflammatory mediators and has been investigated as a potential therapeutic intervention for sepsis.[16–18] However, when tested in randomized controlled studies, continuous hemofiltration at 25 to 30 mL/kg/hr applied at the first sign of organ failure in septic patients, even before severe AKI had developed, did not alter cytokine levels and either did not alter, or worsen, organ function.[19,20] These findings temper enthusiasm for early hemofiltration in septic AKI pending further controlled trials.

The only controlled study to suggest a treatment effect of an RRT clearance mode randomized 206 AKI patients (34% with sepsis) to continuous hemofiltration (25 mL/kg/hr) with or without an added dose of dialysis (18 mL/kg/hr).[21] The group with the added dialysis had greater clearance of urea and creatinine and higher survival rates (34% vs. 59%, $p < .01$). Although this was a single-center study, and the group with added dialysis received higher intensity RRT, it is reasonable to conclude that the combination of clearance modalities is preferable for septic AKI. A multicenter study that examines RRT clearance mode, while standardizing dose, would be required to determine whether this conclusion is valid.

DOSE OF RENAL REPLACEMENT THERAPY

As with any therapy, determining the therapeutic or potential harmful dose of RRT in septic patients is a fundamental consideration.

Dose of Solute Clearance

Traditionally, "dialysis dose" has been determined from urea clearance (Urea Kt/V). Urea is considered to distribute across the volume of total body water (e.g., 60% of body weight), and a "dose" of RRT typically is administered to clear this from an entire volume of total body water (e.g., 42 L in a 70-kg person). However, urea production is variable during critical illness, and it is not known how its clearance specifically relates to removal of other molecules in septic AKI. Given this uncertainty, a more pragmatic dose variable of RRT, particularly for CRRT, is the amount of dialysate plus filtrate replacement fluid applied to create a volume of effluent per hour.

The concept that a higher dose of RRT effluent would enhance recovery from severe AKI has been tested in a number of studies. In a single-center randomized controlled trial of CRRT in 425 patients, survival benefit was seen with effluent rates of 35 to 45 mL/kg/hr compared to 20 mL/

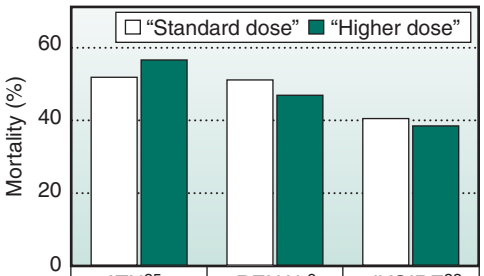
kg/hr (mortality 43% vs. 59%, $p < .01$).[22] Enhanced metabolic clearance and survival advantage with higher intensity RRT also was reported in a single-center German study of 146 patients (36% septic) who were alternately allocated to receive daily or second-daily iRRT. In contrast, other relatively small studies have reported no difference in mortality between groups of patients receiving CRRT with 20 mL/kg/hr effluent compared to 35 to 48 mL/kg/hr.[23,24]

Observational retrospective multinational studies also have reported a lack of survival advantage with higher intensity RRT. In the BEST Kidney study of 1006 patients treated with RRT, median dose of RRT was 20 mL/kg/hr, with only 12% receiving more than 35 mL/kg/hr.[3] The dose of effluent was not independently associated with survival advantage. The Do-Re-Mi study separated 553 patients receiving RRT into more intensive (CRRT ≥ 35 mL/hr/kg, iRRT ≥ 6 sessions per week) and less intensive (CRRT < 35 mL/kg/hr or iRRT < 6 sessions per week), and following multivariate analysis found the higher intensity group appeared to have shorter duration of mechanical ventilation and shorter hospital stay but no difference in ICU mortality.[6] These conclusions were similar when analyzing only those with septic AKI.

There since have been two landmark controlled studies that addressed the dose of RRT applied to patients with severe AKI. The VA/NIH Acute Renal Failure Trial Network randomized patients with severe AKI to intensive (iRRT 6 sessions per week, or CRRT 35 mL/kg/hr) or standard dose RRT (iRRT 3 sessions per week, or CRRT 20 mL/kg/hr).[25] Mode of RRT was stratified according to hemodynamic status and transition between modes was permitted. The study enrolled 1124 patients, of whom 55% had sepsis. Although the higher dose yielded lower serum urea levels, there was no difference in mortality after 60 days (54% vs. 52%, $p = .47$), recovery of renal function, or in the number of days free from organ failure. Analyzing the subgroups with sepsis and those requiring catecholamines also revealed no difference in mortality between groups. The higher dose of RRT appeared safe, and although fluid removal was greater, hypophosphatemia and hypokalemia were more common.

The Randomised Evaluation of Normal versus Augmented Level (RENAL) Replacement Therapy Trial compared effluent flow of 40 vs. 25 mL/kg/hr in 1508 patients, of whom 49% had sepsis.[4] A continuous mode of RRT (filter blood flow ≥150 mL/min) with 50% effluent being dialysate and 50% being ultrafiltrate was used for all patients in the study. The study groups achieved clear separation in administered dose, serum creatinine, and urea, yet there was no difference in mortality, length of stay, or need for ongoing dialysis after 90 days. The conclusions were similar when assessing the group with septic AKI.

Subsequent meta-analyses have concluded that higher doses of RRT in septic AKI (CRRT effluent above 30 mL/kg/hr, or 6 sessions of iRRT per week), provide no survival advantage or recovery in renal function over standard doses of RRT (CRRT effluent < 30 mL/kg/hr or 2–4 iRRT sessions per week)[26] (Fig. 93.1). These findings apply equally to patients with or without sepsis.



	ATN[25]	RENAL[9]	IVOIRE[33]
Year published	2008	2009	2013
Septic (n)/ Total (n)	708/1124	722/1464	137/137
Doses studied (mL/kg/hr)	20 vs 35	25 vs 40	35 vs 70
Mortality outcome	60 days	90 days	28 days

FIGURE 93.1 Mortality rates of the subgroup of patients with septic AKI enrolled in multicenter randomized controlled trials comparing renal replacement therapy (RRT) effluent doses. In all studies, there was no significant difference in survival between groups of septic patients receiving standard or higher-dose RRT.

High-Volume Hemofiltration

High-volume hemofiltration (HVHF) has been defined as a dose of ultra-filtrate exceeding 50 mL/kg/hr using CRRT, or 100 to 120 mL/kg/hr for 4 to 8 hours with iRRT.[27] Enhanced "blood purification" with HVHF has been a popular therapeutic concept after early experimental studies in pigs. Conversely this RRT technique may excessively remove desirable molecules such as micronutrients, anti-inflammatory mediators, and antimicrobials.[28,29]

Pilot studies of HVHF (65 mL/kg/hr) in a small group of patients with sepsis seemed effective and appeared to reduce the dose of noradrenaline that patients were receiving.[30,31] Subsequent controlled trials, which included 64 septic AKI patients, showed this technique was safe but could not demonstrate a clear benefit.[32]

The multicenter IVOIRE Study (High Volume in Intensive Care Trial) randomized 140 patients with septic AKI to receive 35 or 70 mL/kg/hr continuous hemofiltration through a polyethersulfone filter (with 35 kD cutoff pore size) for 96 hours.[33] These patients had severe disease and were receiving high doses of catecholamines. Sepsis originated from the abdomen in 50%, lung in 25%, and two thirds had a Gram-negative infection. The HVHF group had higher clearance yielding lower serum creatinine and urea, but there was no difference in 28-day mortality. Even though the study did not recruit the desired number of patients and was underpowered for its primary endpoint, there was not even a trend to difference in duration of ventilation, length of stay, duration of RRT, catecholamine-free days, or any endpoint of organ dysfunction, even when adjusted for severity of illness. It is concerning that hypophosphatemia and antibiotic clearance was markedly higher with HVHF despite a treatment protocol to prevent this.

Extra high-volume hemofiltration (50 vs. 85 mL/kg/hr) has been tested in 280 patients with septic AKI, but yielded no change to survival or any other patient-centered outcome.[34] The lack of efficacy of HVHF on mortality, hospital length of stay, renal recovery, and hemodynamic status has been noted in meta-analysis of four controlled trials involving a total of 466 patients.[35] Interestingly, the recent HEROICS study of HVHF (80 mL/kg/hr) in shocked cardiac surgical patients on high-dose catecholamine infusion reported no difference in mortality or length of hospital stay.[36]

Dose of Fluid Removal

Retrospective studies have identified that patients with AKI have higher mortality if they have a positive fluid balance.[37,38] In a posthoc analysis of the RENAL Study, half of the patients had a positive mean daily fluid balance, and this group of

patients had a 70% higher mortality rate, more time on RRT, mechanical ventilation, and longer lengths of stay. This observation remained significant even after adjusting for severity of illness and excluding the fluid balance in the first 2 days of RRT.[39] An association between fluid balance and outcomes also has been illustrated in patients with sepsis.[40] In the ARDSnet study, those patients with lung disease administered lower volumes of parenteral fluids developed less AKI, and fewer patients required RRT.[41] Taken together, these observations should encourage careful consideration to the dose of fluid removal applied to patients with septic AKI on RRT and support the avoidance of accumulating positive fluid balance.

Dose of Therapeutic Agents

Therapeutic drug monitoring is important to consider when applying RRT for septic AKI. β-lactams, glycopeptides, and aminoglycoside readily pass across RRT membranes and require dose adjustment. Reference guides are available for these dose adjustments.[42] Such references should be consulted carefully, especially if high volume hemofiltration is applied.

FILTER MEMBRANES

Filters used in RRT circuits are characterized by their composition, biocompatibility, pore size, surface area, and flux. Biocompatible synthetic membranes that have very little complement activation have been a major advancement in RRT technology and have resulted in lower rates of death than use of cellulose membranes. In the BEST Kidney study, the most commonly used filter was composed of polyacrylonitrile, polysulfone, or polyamide. Although not specifically reported in the septic AKI subgroup, the type of filter used was not an independent predictor of mortality.[3]

Current synthetic filters allow flux of molecules up to 30 to 40 kD, theoretically permitting extraction of most inflammatory mediators. However, plasma levels of most cytokines are unchanged with RRT, even with very high ultrafiltration rates. High cutoff membranes allowing filtration of molecules up to 60 kD are thought to further enhance clearance of molecules involved with sepsis. In preclinical and pilot clinical studies, RRT using these filters appeared to allow earlier reduction of noradrenaline doses in septic AKI.[43] However, a subsequent larger study of high cutoff membranes in sepsis (HICOSS) was stopped after enrolment of 81 patients, because there was no survival benefit, reduction in catecholamines, mechanical ventilation, or length of stay.[27]

A range of new filters has been developed (e.g., AN69 surface treated ST, SEPTEX, polymethyl-methacrylate, Oxiris, polymyxin B, and CytoSorb). These currently are being tested to determine if they attenuate the severity of sepsis, rather than primarily improve outcome in septic AKI.

TIMING OF RENAL REPLACEMENT THERAPY

Absolute indications for RRT include life-threatening hyperkalemia, uremic complications, severe metabolic acidosis, intoxication with dialyzable substances, and excessive interstitial fluid (e.g., pulmonary edema).[44] When to commence RRT in septic AKI has been a matter of debate and variable practice.[3] RRT may confer some theoretical advantages in septic AKI, and commencing it early in disease may attenuate severity of illness. However, initiating RRT unnecessarily may risk complications from catheter insertion, metabolic correction, clearance of therapeutic substances, and impaired recovery of renal function.

There have been conflicting reports from retrospective observational studies regarding the benefits of commencing RRT earlier in disease. From the BEST Kidney study, those patients who had RRT started later in time or later in disease (i.e., with higher serum creatinine) had lower rates of renal recovery.[45] A single-center retrospective study of 147 septic AKI patients separated the cohort into those who received RRT when serum urea was less than 36 mmol/L (early) or 36 mmol/L or more (late).[46] Although mortality was significantly lower in the group started RRT early (52% vs. 68%, $P < .05$), the dose and adequacy of RRT were not considered, and more than twice as many patients who started late RRT had cancer, suggesting a treatment selection bias. Another retrospective analysis, assessing RRT timing in the RENAL study, examined a subgroup of 439 patients, 53% of whom had sepsis. Multivariate analysis revealed no significant relationship between time to initiate RRT and mortality, duration of mechanical ventilation, ICU length of stay, or renal recovery. Interestingly, those without absolute indications for RRT (i.e., hyperkalemia, severe acidosis, edema) and patients with higher serum creatinine levels tended to have higher survival rates when renal supports were commenced later.[47]

Meta-analysis of studies that reported time to RRT initiation concluded that there was a lower rate of mortality and a trend to less dependence on chronic dialysis in the groups of patients receiving earlier RRT. However, data were derived largely from small, historical, uncontrolled studies with marked publication bias, different definitions of renal failure, variable timing of RRT, and with uncertain relevance to septic patients.[48,49] Controlled studies clearly are needed to clarify the optimal timing of RRT in septic AKI.

A small controlled study examined the effect of applying the same dose of hemofiltration early or later in 71 patients with severe AKI. RRT was applied a mean of 7 hours after randomization in the early group, and after 42 hours in the delayed group. There was no difference in mortality rates, hospital length of stay, or renal recovery between groups, including patients with sepsis.[23]

The Artificial Kidney Initiation in Kidney Injury (AKIKI) trial was a French multicenter, prospective, open-label randomized controlled trial on ICU patients receiving catecholamines or mechanical ventilation and with severe AKI (serum creatinine > 354 nmol/L or greater than three times baseline, anuria for more than 12 hours, or oliguria for more than 24 hours) with no absolute indication for RRT (i.e., oliguria for more than 72 hours, or urea > 40 mmol/L, or serum potassium > 6 mmol/L, or pH < 7.15, or diuretic resistant pulmonary edema).[7] Patients were randomized to receive any mode of RRT immediately upon satisfying enrolment criteria or to wait and be closely monitored until an absolute indication was encountered. The AKIKI trial enrolled 602 patients, 80% with sepsis, with early and delayed RRT groups evenly matched at baseline. Of the 308 patients randomized to receive expectant management, only 157 (51%) received RRT, at a median of 57 hours after randomization. Despite evolution of more marked metabolic derangement in the delayed group, mortality rates at day 60 were similar between early and delayed RRT groups (49% vs. 50%, $p = .79$). Secondary end points including lengths of stay, days on catecholamines, and measures of organ dysfunction did not differ between

groups. Patients allocated to delayed RRT had fewer catheter-related infections, less hypophosphatemia, and an earlier spontaneous diuresis. Although the subgroup of patients with septic AKI were not analyzed separately, they accounted for the vast majority of patients enrolled and hence the outcomes are likely to apply to this group.

Although this study indicates that early RRT provides no clear benefit for all patients with severe AKI, mortality rates were highest in those who received delayed RRT (62%) compared with those who were allocated to delayed RRT but did not require it (37%). It is further concerning that mortality was higher in those who received early RRT (49%) than those who never received RRT (37%). Although these differences in mortality rates were not significant after adjusting for severity of illness, it supports the need to investigate for better markers to determine which septic patients with AKI will benefit from early, delayed, or no RRT at all.

The Early versus Late Initiation of Renal Replacement Therapy in Critically Ill Patients with Acute Kidney Injury (ELAIN RCT) was published soon after.[50] This single-center German study enrolled 231 patients with Kidney Disease: Improving Global Outcomes (KDIGO) stage 2 AKI, neutrophil gelatinase-associated lipocalin (NGAL) greater than 150 ng/mL, or those with septic shock. Patients were randomized to start RRT within 8 hours (early) or within 12 hours of developing KDIGO stage 3 AKI (delayed), with the mode and dose of RRT the same for both groups (CVVHDF at 30 mL/kg/hr using citrate anticoagulation). All patients assigned early RRT received it, whereas 9% assigned delayed therapy did not receive it. The delayed group had a higher mortality at 90 days than the group that received earlier RRT (55%, vs. 39%, $p = .03$). Secondary end points also differed, with the early group having shorter duration of RRT, mechanical ventilation, and a hospital length of stay that was reduced by 30 days. Although there are many strengths of this study, the delayed group appeared to have higher Acute Physiology and Chronic Health Evaluation (APACHE) and NGAL at baseline, and there was no adjustment for these confounders. Most of the AKI in this study followed cardiac surgery and the 32% of enrolled patients having sepsis were not analyzed separately. The separation between groups in the time to commence RRT was only modest and would be unlikely to account for the absolute mortality reduction of 16% and the 1-month shorter hospital stay. Nevertheless, this study supports the need for a further multicenter study that tests the effect of RRT timing while controlling how this therapy is applied.

Of relevance to this debate regarding optimal timing of RRT in severe septic AKI, the HEROICS trial of early HVHF in cardiac surgical patients on high-dose catecholamines, reported no change in mortality, and that 43% of the patients assigned to expectant management did not require RRT. Although this study was not conducted in septic patients, it supports a watch-and-wait approach even in severe shock.[36]

Two further trials are underway to determine the clinical outcomes of commencing RRT at different times. The Standard versus Accelerated Initiation of Renal Replacement Therapy in Acute Kidney Injury (STARRT-AKI) trial is an international multicentre study of patients with severe AKI randomized to receive RRT (any mode) within 12 hours or at the discretion of the clinician. A pilot study of 101 patients (57 with sepsis) found no difference in mortality with timing of RRT.[51]

The effect of RRT timing in septic AKI will be studied in the Initiation of Dialysis Early versus Delayed in the Intensive Care Unit (IDEAL-ICU).[52] In this French study, patients with severe AKI (RIFLE-F stage) in early septic shock will be enrolled within 48 hours of commencing catecholamines. Any mode of RRT is allowed with doses of at least 25 mL/kg/hr (or iRRT at least every 2 days for 4–6 hours). Trial investigators plan to recruit 864 patients to determine if RRT within 12 hours or delayed RRT will provide mortality benefit, renal recovery, and influence long-term outcomes.

A remaining uncertainty regarding timing of RRT is the best prompt for starting this therapy. Besides the absolute indications of RRT described earlier, serum urea, serum creatinine and urine output have been the usual parameters used to guide when therapy should be commenced. However, serum urea and creatinine are imprecise biomarkers of renal function because they have variable rates of production during critical illness and may not necessarily reflect kidneys that are injured enough to require RRT support. Renal biomarkers such as NGAL, tissue inhibitor of metalloproteinases (TIMP), and insulin-like growth factor binding protein-7 (IGFBP7) are being investigated to determine if these are better triggers to commence RRT in septic AKI.[53] Their specific relevance to patients with septic AKI remains unclear.

SUMMARY

Based on current evidence, the choice of intermittent or continuous RRT for septic AKI is best determined by the patient's condition and local expertise with available technology. For patients with septic AKI requiring pharmaceutic support of blood pressure, continuous RRT modes may be preferable, whereas in hemodynamically stable patients (a minority), intermittent modes of RRT may be acceptable. There is currently little evidence to guide whether dialytic or convective clearance is most efficacious in septic AKI or what constitutes optimal timing of intervention; however, volume control appears important. Newer approaches such as HVHF and high cutoff membranes have not produced any clinical benefits and remain research tools.

RRT effluent doses of 25 mL/kg/hr appear suitable for severe septic AKI. Effluent doses beyond this are not associated with any benefit and have led to greater incidence of hypophosphatemia, hypokalemia, antibiotic clearance, and increased costs. Although higher doses have not proven beneficial, clinicians should be aware that prescribed doses may not be achieved if RRT repeatedly is interrupted (e.g., filter clotting, patient transport) or if doses are not adjusted for patient size.

If there are no absolute indications to commence RRT in septic AKI, there appears no compelling evidence to support earlier initiation. An expectant approach, while closely monitoring electrolytes, pH, volume status, and uremia, appears appropriate. In the meantime, research should focus on determining other parameters that may indicate when RRT is beneficial.

Key Points

1. Patients receiving renal replacement therapies (RRT) for septic acute kidney injury (AKI) have markedly high mortality rates (40% to 70%).
2. Current evidence suggests that preemptively commencing RRT for septic AKI does not confer survival advantage or enhance renal recovery.

3. Continuous and intermittent modes of RRT appear equally effective for septic AKI. The impact of RRT mode on hemodynamics must be considered.
4. There is no clinical advantage of providing continuous RRT effluent doses beyond 25 mL/kg/hr, or more than three intermittent RRT sessions per week.
5. High-volume hemofiltration and increased porosity of filter membranes have yielded no clinical benefit for patients with septic AKI.

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