Blood Purification

Blood Purif 2001;19:227–232

Indications for Dialysis in the ICU: Renal Replacement vs. Renal Support

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Introduction

Whether or not to provide dialytic support, and if so, when, are two of the most fundamental questions facing nephrologists and intensivists in most cases of acute renal failure (ARF) in the ICU. Although these decisions are integral to the management of any critically ill patient with renal failure in the ICU, there is limited information on what should determine the decision to dialyze. Over the last decade significant advances have been made in the availability of different dialysis methods for replacement of renal function. The advances have ranged from modifications in intermittent dialysis, e.g. biocompatible membranes, bicarbonate dialysate and smarter dialysis machines with volumetric ultrafiltration controls, to the development of several modalities for continuous renal replacement therapy (CRRT) [1–6]. Several of these techniques may be used to treat ARF in the ICU, but there is little information on when dialysis should be offered and which therapies are most appropriate in a given circumstance. This article outlines the current concepts in the use of dialysis techniques for ARF in the ICU and suggests an approach for providing dialysis support for the critically ill patient.

Dialysis Decisions in the ICU: Current Practice

In general, most nephrologists will have no hesitation in offering dialysis in the presence of life-threatening situations, e.g. severe hyperkalemia, marked acid-base disturbances or diuretic-resistant pulmonary edema. However, in the absence of these factors there is generally a tendency to avoid dialysis as long as possible, a thought process that reflects the decisions made for patients with end-stage renal disease, in whom the initiation of dialysis signals the start of dialysis dependency. Two factors tend to dissuade nephrologists from initiating dialysis in the ICU. First, there are well-known risks of the dialysis procedure, including hypotension, arrhythmia, and complications of vascular access placement. Second, there is a strong concern that some element of the dialysis procedure may slow the recovery of renal function, and increase the risk of developing end-stage renal failure [7–9]. This contention is supported by experimental data showing renal lesions consistent with fresh ischemia in animals dialyzed without systemic hypotension, long after their initial renal injury. Thus, in current practice, the decision to dialyze is based most often on clinical features of volume overload and biochemical features of solute imbalance (azotemia, hyperkalemia) [10–12].

As shown in figure 1, the decision to dialyze is often based on an estimation of the likelihood for and timing of renal functional recovery. Factors that influence the likelihood of renal functional recovery include a knowledge of the nature and timing of renal insult, the severity of the underlying illness and associated co-morbidities and the presence of other factors known to adversely influence renal function, e.g. prolonged hypotension (table 1). When the nature and timing of the renal insult is known,

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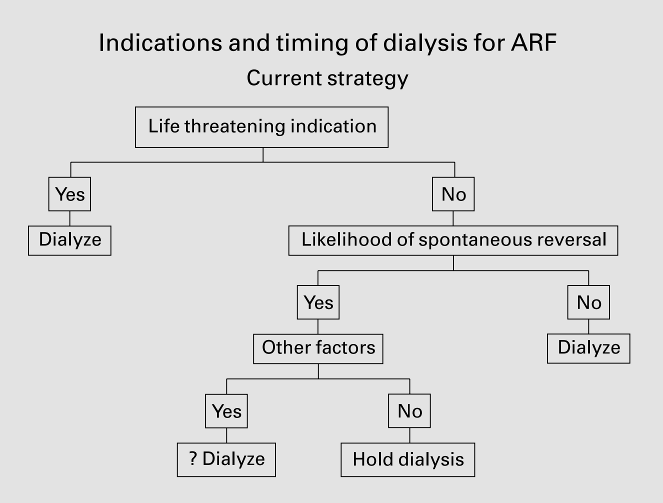

Fig. 1. Decision process for initiation of dialysis in the ICU.

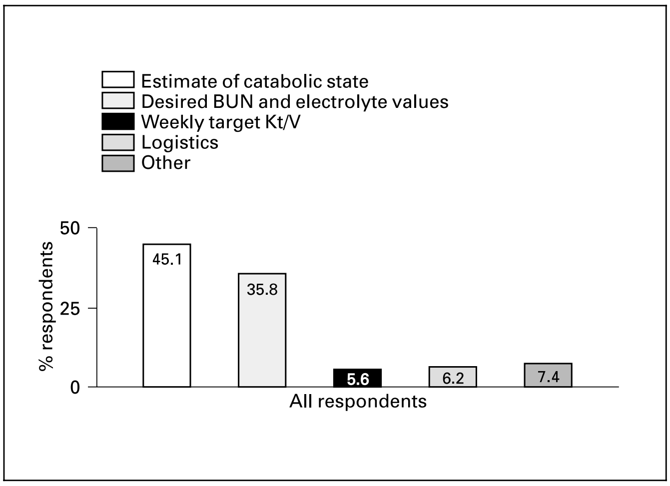

Fig. 2. Factors affecting initial timing and frequency of dialysis. Results from a survey of US nephrologists.

Table 1. Factors to assess likelihood of spontaneous reversal of renal dysfunction in ARF

Factor	Influence
Nature and timing of renal insult	Both nature and timing well defined, e.g. antibiotic nephrotoxicity (20%) Possible knowledge of insult and timing, e.g. postoperative ARF (30%) Nature and timing unknown, e.g. multiorgan failure (50%)
Presence of oliguria	Affected by diuretic use Inaccurate marker for estimating level of renal function Unreliable as an indicator for recovery
Change in BUN and creatinine	Affected by multiple factors Imprecise in detecting impending recovery May lag behind recovery
Underlying disease	Is ARF an epiphenomenon? Does ARF contribute to outcome?
Other factors	Demand exceeds renal excretory capacity, e.g. volume resuscitation Intensivist demand Logistics

e.g. a contrast load during an angiographic procedure, it may be possible to estimate the duration of renal dysfunction and withhold dialysis until evidence of worsening or improvement is obtained. In most circumstances, however, the nature and timing of renal injury are not precisely determined and it is thus difficult to predict the course. Most clinicians base their estimate of the severity of renal dysfunction on the presence or absence of oliguria, the rate of change in blood urea nitrogen (BUN) and knowledge of the underlying disease. A recent survey of practicing nephrologists showed that the main determinants for the timing of intervention were an estimate of catabolic state and a need to treat specific levels of BUN (level >100 mg/dl) (fig. 2) [13]. Unfortunately, these parameters are subject to wide variation and do not always reflect the underlying state.

While oliguric renal failure has been associated with a poor outcome in most studies and dialyzed patients are more likely to be oliguric, urine volume is influenced by diuretic use and is an inaccurate marker of renal function and is unreliable as an indicator for impending renal recovery. Similarly the change in BUN and creatinine is influenced not only by the change in renal function but also by the underlying volume status, catabolic state and nutritional supplementation. Thus these markers become inaccurate to estimate changes in renal function and may lag behind recovery. Some other factors that influence the decision to dialyze include volume requirement in excess of urinary output, demand from the consulting physician to provide dialysis and the availability of dialysis based on logistical issues. It is thus evident that at the current time there is no standardization of the indications or timing of dialysis in the ICU and in most instances the decision to offer dialysis uses a thought process similar to that used for ESRD. I believe that this approach is problematic and fails to recognize the varying needs of the critically ill patient and thereby limits the application of dialysis techniques.

Dialysis Decisions in the ICU: Need for Change?

It is quite evident that despite the availability of several dialysis techniques, including CRRT, we have been unable to demonstrate an improvement in survival in critically ill patients who develop ARF in the ICU setting. While several factors influence survival from ARF, there is emerging evidence that the development of ARF itself imparts a significant risk for an adverse outcome. Levy et al. [14] found a fivefold increased risk of mortality in patients who developed contrast-induced ARF in comparison to those who did not. The increased risk could be attributed to worsening of pre-existing and development of new onset sepsis, respiratory failure, mental status changes and bleeding. Similarly, Chertow et al. [15] found 30-day mortality in patients with ARF post-cardiac surgery was 63.7% compared with 4.3% in patients without ARF. Most recently, Vincent et al. [16] have shown that ICU mortality was three times higher in patients with ARF and that these patients had a greater incidence of infections and multiorgan failure. We have previously shown that the time to consultation for ARF and institution of therapy has a significant effect on mortality, renal functional recovery and length of stay in the ICU [17]. Thus these studies all support the notion that if ARF is unrecognized or untreated it contributes to an adverse outcome.

If ARF is deleterious, it is tempting to postulate that earlier intervention with dialysis may be of benefit; however relatively few studies have carefully examined this question [18–22] (none in the modern dialysis era), and most studies on timing are confounded by differences in intensity as a result of a chosen therapeutic strategy. Moreover, changes in the severity of illness, especially in later years, make comparisons of studies extremely difficult. Conger [21] and Gillum et al. [22] performed prospective studies of the intensity of dialysis, the former showing beneficial trends in improved survival, although neither were well controlled for timing of intervention. Case mix clearly differs today compared with these studies dating back several decades. A much smaller proportion of patients require dialysis because of obstetric complications, and many more are elderly and suffer from multiple organ dysfunction accompanying ARF. Furthermore, what was considered early in the previous studies would not be considered early by most criteria today. Many modern nephrologists intervene when the serum urea nitrogen concentration is in excess of 100 mg/dl, for fear of impending uremic complications.

Our data from a randomized controlled trial comparing intermittent hemodialysis (IHD) to CRRT [23] suggest that the indication for dialysis is an important determinant of outcome. In our trial, patients who were dialyzed predominantly for solute control had a better outcome than those who were dialyzed predominantly for volume overload. Patients dialyzed for control of both azotemia and volume overload experienced the worst outcome. Mukau et al. [24] found that 95% of their patients with postoperative ARF had fluid excess of more than 10 liters at the time of dialysis. The amount of fluid overload was a strong determinant of outcome independent of other factors. Volume resuscitation is a common strategy used in the treatment of multiple organ dysfunction, particularly when accompanied by sepsis syndrome and hypotension. It is often applied indiscriminately in the setting of oliguric ARF, where it is assumed that providing additional volume will lead to increased renal perfusion, and prompt correction of renal dysfunction. While this may be of great benefit in patients with prerenal azotemia, excessive fluid administration can lead to pulmonary edema, compromising oxygenation and ventilation, and may hasten the need for dialysis. These factors collectively suggest that we need to develop evidence-based, patient-specific, nonbiased indications for the initiation of dialysis in ARF.

Dialysis in the ICU: Suggested Approach

We favor utilizing an approach that recognizes that critically ill patients have different needs than stable patients with ESRD and that dialysis in the ICU can serve several purposes. The following factors should be considered in defining the indications and timing of dialysis.

Characteristics of the Critically Ill Patient

When ARF complicates the course of a critically ill patient in the ICU it is usually associated with multiple organ failure (MOF), which can influence the course of the patient in two ways. There may be a rapid decline of renal function that does not permit much of an adaptive response, which characterizes the course of the patient with ESRD. Second, therapeutic interventions designed to support other organ function, e.g. volume resuscitation, may exceed the renal excretory capacity, contributing to a worsening of the underlying state. In these circumstances it is apparent that the goal for any therapeutic intervention is to provide support for various organs and compensate for the adverse effects of other therapeutic interventions to provide an opportunity for the patient to recover from the underlying illness. Renal functional recovery is thus largely influenced by recovery of other organ func-

Table 2. Strategies for management of renal failure

	ARF	ESRD
Goals of therapy	Improve organ system failure	Ameliorate uremia
Desired outcome	Survival, recovery of renal function	Long-term survival, quality of life
Determining factor	Other organ function	Renal process
Indication for dialysis	Renal support	Renal replacement

Table 3. The changing paradigm of dialysis in the ICU

	Renal replacement	Renal support
Purpose	Replace renal function	Support other organs
Timing of intervention	Based on level of biochemical markers	Based on individualized need
Indications for dialysis	Narrow	Broad
Dialysis dose	Extrapolated from ESRD	Targeted for overall support
Application	Renal failure	Renal and nonrenal indications

tion. Dialysis in this setting thus has the primary goal to provide adequate renal support for other organ function. This is in contrast to the patient with ESRD in whom the goal for dialysis is to ameliorate the effects of uremia and the determinant for long-term outcome is primarily the delivery of dialysis (table 2).

Goals of Therapy and Therapeutic Potential of Dialysis

The broad goals for treating ARF with dialysis are to (1) maintain fluid and electrolyte, acid-base and solute homeostasis, (2) prevent further insults to the kidney, (3) promote healing and renal recovery and (4) permit other support measures (e.g. nutrition) to proceed without limitation. Dialysis techniques differ in their operational characteristics and their ability to provide renal support and this should be considered in the dialysis decision. For instance, dialysis is largely viewed as a method to remove solute and fluids, as these are the main options utilized for ESRD patients. However, in the ICU setting dialysis techniques could be used not only to remove substances but also to add them and selectively manipulate the internal milieu. For instance, CRRT techniques can be successfully utilized for fluid regulation [25], selective replacement of specific electrolytes, e.g. bicarbonate, without the addition of sodium or fluid [26] or to add substances back to the blood [27]. Similarly the use of combined techniques (e.g. combined plasma filtration adsorption for sepsis, cell-based and hemoperfusion devices for hepatic support devices) is emerging [28–31]. As a consequence, the traditional indications for renal replacement may need to be redefined. For instance, excessive volume resuscitation, a common strategy used for MOF, may be an indication for dialysis even in the absence of significant elevations in BUN. In this respect it may be more appropriate to consider dialytic intervention in the ICU patient as a form of renal support rather than renal replacement (table 3). This terminology serves to distinguish between the strategy for replacing individual organ function and one to provide support for all organs. Table 4 lists some of the revised

Table 4. Potential indications for dialysis in critically ill patients

Renal replacement	
Life-threatening indications	Hyperkalemia
	Acidemia
	Pulmonary edema
	Uremic complications
Solute control	
Fluid removal	
Regulation of acid-base and electrolyte status	
Renal support	
Nutrition	
Fluid removal in congestive heart failure	
Cytokine manipulation in sepsis	
Cancer chemotherapy	
Treatment of respiratory acidosis in ARDS	
Fluid management in multiorgan failure	

Table 5. Renal replacement therapy for ARF: initial choice

Indication	Clinical setting	Modality
Uncomplicated ARF	Antibiotic nephrotoxicity	IHD, PD
Fluid removal	Cardiogenic shock, CP bypass	SCUF, CVVH
Uremia	Complicated ARF in ICU	CRRT (CVVHD, CVVH, CVVHDF), IHD
Increased intracranial pressure	Subarachnoid hemorrhage, hepatorenal syndrome	CRRT (CVVH, CVVHDF)
Shock	Sepsis, ARDS	CRRT (CVVH, CVVHDF)
Nutrition	Burns	CRRT (CVVHD, CVVHDF, CVVH)
Poisons	Theophylline, barbiturates	Hemoperfusion, IHD, CVVHD
Electrolyte abnormalities	Marked hyperkalemia	IHD, CVVHD

indications for dialytic intervention using this approach. It is thus possible to widen the indications for renal intervention and provide a customized approach for the management of each patient. It is also apparent that this approach will become increasingly the norm as we move into the era of using dialysis for nonrenal problems [32–33].

Recommendations for Initial Choice of Dialysis in the ICU

Despite the lack of definitive results derived from randomized clinical trials [34], it is possible to develop a rational approach to the selection of a dialysis modality for the initial treatment of ARF in critically ill patients. A primary consideration is the availability of a technique at the center and familiarity and comfort of personnel with the technique. The latter point is extremely important with respect to continuous techniques as infrequent use may be associated with a higher incidence of iatrogenic complications [35, 36]. The next consideration is the complexity of the patient, the location in the hospital and need for mobility.

Patients with uncomplicated ARF can be treated with IHD or acute peritoneal dialysis (APD) and the choice between these is based on other patient characteristics (e.g., pregnancy, hemodynamic tolerance, access and urgency for treatment). Patients with MOF and ARF can be treated with CRRT or IHD. In general, hemodynamically unstable, catabolic and excessively fluid overloaded patients are ideally treated with CRRT, whereas IHD may be better suited for patients requiring early mobilization and who are more stable. Table 5 depicts a potential therapy for several different clinical scenarios. Amongst continuous therapies, those that include hemofiltration (CVVH, CVVHDF) may be superior in sepsis or the systemic inflammatory response syndrome because of the ability to more efficiently remove larger molecular weight solutes [23, 37]. For most clinical scenarios, we favor the use of hemodiafiltration techniques that combine dialysis and ultrafiltration and thus are ideal for both small and large molecule clearances [37, 38]. It is important to stress that one of the key factors in the choice of renal replacement is to tailor the therapy to the patient. This implies an ongoing assessment of the patient and modification of the therapy used based on clinical criteria (e.g., in a hemodynamically unstable patient CRRT may be an initial choice, however, when the patient is more stable and needs to be mobilized IHD may be more appropriate). We would suggest that flexibility in utilizing the entire range of renal replacement therapies is an important adjunct to the management of ARF.

In summary, management of ARF in the ICU is different from that of ESRD and the dialysis prescription should incorporate the unique characteristics of each patient. Several new methods of dialysis are now available to treat ARF. The application of these techniques is rapidly expanding. Rational use of these techniques should be based on the overall concept of providing renal support. The choice of therapy requires an understanding of the therapeutic potential of a modality and appreciation of the advantages and disadvantages of each technique. Therapeutic alternatives to traditional IHD now permit nephrologists to match the method to the patient. This approach will allow better management of ARF patients and may improve outcome.

References

1 Mallick NP, Gokal R: Haemodialysis. Lancet 1999;353:737–742.
2 Briglia A, Paganini EP: Acute renal failure in the intensive care unit. Therapy overview, patient risk stratification, complications of renal replacement, and special circumstances. Clin Chest Med 1999;20:347–366.
3 Canaud B, Bosc JY, Leray H, Stec F, Argiles A, Leblanc M, Mion C: On-line haemodiafiltration: State of the art. Nephrol Dial Transplant 1998;13(suppl 5):3–11.
4 Ronco C: Haemodialysis filters: What's new? Curr Opin Nephrol Hypertens 1999;8:709–713.
5 Leblanc M, Moreno L, Robinson OP, Tapolyai M, Paganini EP: Bicarbonate dialysate for continuous renal replacement therapy in intensive care unit patients with acute renal failure. Am J Kidney Dis 1995;6:910–917.
6 Manns M, Sigler MH, Teehan BP: Continuous renal replacement therapies: An update. Am J Kidney Dis 1998;32:185–207.
7 Adams PL, Adams PF, Bell PD, Navar LG: Impaired renal blood flow autoregulation in ischemic acute renal failure. Kidney Int 1980; 18:68–76.
8 Conger J: The role of blood flow autoregulation in pathophysiology of acute renal failure. Circ Shock 1983;11:235–244.
9 Conger JD: Does hemodialysis delay recovery from acute renal failure? Semin Dial 1990;3: 146–147.
10 Bellomo R, Ronco C: Indications and criteria for initiating renal replacement therapy in the intensive care unit. Kidney Int Suppl 1998;66: S106–S109.
11 Star RA: Treatment of acute renal failure. Kidney Int 1998;54:1817–1831.
12 Paganini EP: Dialysis is not dialysis is not dialysis! Acute dialysis is different and needs help! Am J Kidney Dis 1998;32:832–833.
13 Mehta RL, Letteri J: Renal replacement therapy for ARF, current trends: A survey of US Nephrologists. Am J Nephrol 1999;19:377–382.
14 Levy EM, Viscoli CM, Horwitz RI: The effect of acute renal failure on mortality. A cohort analysis JAMA 1996;275:1489–1494.
15 Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J: Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104: 343–348.
16 de Mendonca A, Vincent JL, Suter PM, Moreno R, Dearden NM, Antonelli M, Takala J, Sprung C, Cantraine F: Acute renal failure in the ICU: Risk factors and outcome evaluated by the SOFA score. Intensive Care Med 2000; 26:915–921.
17 Mehta RL, Farkas A, Fowler W, Pascual M: Effect of delayed consultation on outcome from acute renal failure in the ICU (abstract). 28th Annual Meeting of the American Society of Nephrology, Nov 1995.
18 Parsons FM, Hobson SM, Blagg CR, McCracken BH: Optimum time for dialysis in acute reversible renal failure. Description and value of an improved dialyzer with large surface area. Lancet 1961;i:129–134.
19 Fischer RP, Griffen WO, Reiser M, Clark DS: Early dialysis in the treatment of acute renal failure. Surg Gynecol Obstet 1966;123:1019–1023.
20 Kleinknecht D, Jungers P, Chanard J, Barbanel C, Ganavel D: Uremic and non-uremic complications in acute renal failure: Evaluation of early and ferquent dialysis on prognosis. Kidney Int 1972;1:190–196.
21 Conger JD: A controlled evaluation of prophylactic dialysis in post-traumatic acute renal failure. J Trauma 1975;15:1056–1063.
22 Gillum DM, Dixon BS, Yanover MJ, Kelleher SP, Shapiro MD, Benedetti RA, Dillingham MI, Paller MS, Goldberg JP, Tomford R, Gordon JA, Conger JD: The role of intensive dialysis in acute renal failure. Clin Nephrol 1986;25: 249–255.
23 Mehta RL, McDonald B, Pahl M, Farkas M, Pascual M, Fowler B and the ARF Collaborative Study Group: Continuous vs. intermittent dialysis for acute renal failure in the ICU: Results from a randomized multicenter trial. J Am Soc Nephrol 1996;7:1456.
24 Mukau L, Latimer RG: Acute hemodialysis in the surgical intensive care unit. Am Surg 1988; 54:548–552.
25 Mehta RL: Fluid management in continuous renal replacement therapy. Semin Dial 1996;9: 140–144.
26 Kierdorf HP, Leue C, Arns S: Lactate- or bicarbonate-buffered solutions in continuous extracorporeal renal replacement therapies. Kidney Int 1999;56(suppl 72):S32–S36.
27 Ronco C, Ghezzi PM, La Greca G: The role of technology in hemodialysis. J Nephrol 1999; 12(suppl 2):S68–S81.
28 Schetz M, Ferdinande P, Van den Berghe G, Verwaest C, Lauwers P: Removal of proinflammatory cytokines with renal replacement therapy: Sense or nonsense? Intensive Care Med, 1995;21:169–176.
29 Tetta C, Bellomo R, Brendolan A, Piccinni P, Digito A, Dan M, Irone M, Lonnemann G, Moscato D, Buades J, La Greca G, Ronco C: Use of adsorptive mechanisms in continuous renal replacement therapies in the critically ill. Kidney Int 1999;56(suppl 72):S15–S19.
30 Ronco C, Brendolan A, Dan M, Piccinni P, Bellomo R, De Nitti C, Inguaggiato P, Tetta C: Adsorption in sepsis. Kidney Int 2000;58(suppl 76):S148–S155.
31 Rahman TM, Hodgson HJ: Review article: Liver support systems in acute hepatic failure. Aliment Pharmacol Ther 1999;13:1255–1272.
32 Schetz M: Non-renal indications for continuous renal replacement therapy. Kidney Int 1999;56(suppl 72):S88–S94.
33 Tetta C, Ronco C, Brendolan A, Irone M, Digito A, Cioffi M, Piccinni P, Dan M, Inguaggiato P, La Greca G: Present and future options in continuous renal replacement therapies of sepsis and MOF. Minerva Anestesiol 1999;65: 419–426.
34 Mehta RL, McDonald B, Pahl M, Farkas M, Pascual M, Fowler B and the ARF Collaborative Study Group: Continuous vs. intermittent dialysis for acute renal failure in the ICU: Results from a randomized multicenter trial. Kidney Int, in press.
35 Manns M, Sigler MH, Teehan BP: Intradialytic renal haemodynamics – Potential consequences for the management of the patient with acute renal failure. Nephrol Dial Transplant 1997;12:870–872.
36 Mehta RL: Renal replacement therapy for acute renal failure: Matching the method to the patient. Semin Dial 1993;6:253–259.
37 Clark WR, Mueller BA, Kraus MA, Macias WL: Dialysis prescription and kinetics in acute renal failure. Adv Renal Replace Ther 1997;4 (suppl 1):64–71.
38 Bellomo R, Ronco C: Acute renal failure in the intensive care unit: Adequacy of dialysis and the case for continuous therapies Nephrol Dial Transplant 1996;11:424.