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Adequacy of Dialysis in Acute Renal Failure

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Renal replacement therapy (RRT) is currently the mainstay of management for patients with acute renal failure (ARF). Adequacy of dialysis in the setting of renal failure is defined poorly and encompasses multiple domains of clinical and biochemical outcomes. Multiple operational factors influence the delivery of adequate dialysis. No current standards exist for RRT for ARF; current RRT practices for ARF generally have been extrapolated from end-stage renal disease (ESRD) literature. The heterogeneity of patient population, variation in RRT practices, and differences in outcomes studied have made it difficult to define or study adequate dialysis in ARF or its impact on clinical outcomes.
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Acute renal failure (ARF) occurs in as many as 15% of critically ill patients and is associated with significant morbidity and mortality. Despite the common occurrence and high morbidity and mortality associated with ARF, no pharmacologic interventions are efficacious in its treatment. Supportive care, including renal replacement therapy (RRT), remains the mainstay of management for critically ill patients with ARF. The mortality rate associated with ARF requiring RRT has remained in excess of 50%,[1] despite advances in the use of RRT.[2-5] This is partly owing to the fact that our understanding on how best to provide RRT for patients with ARF even after a half-century of clinical use is limited.

In patients with end-stage renal disease (ESRD), delivering adequate dialysis consistently has been shown to improve clinical outcomes.[6-8] Even in this setting, controversy exists as to how to define, prescribe, deliver, and measure the adequacy of dialysis. One can argue that patients with ARF are far more ill, malnourished, and catabolic than ESRD patients, and hence warrant more RRT. However, very little attention has been paid to the concept of adequate dialysis in the ARF setting. This is confounded further by the heterogeneity of the patient population, different modalities of RRT available for ARF, and huge variations in RRT practices across centers.

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Adequate Dialysis in the ARF Setting

The term *adequate dialysis* is defined poorly. Although it may encompass success in achieving various clinical and/or biochemical outcomes, adequacy of dialysis most commonly is defined in terms of urea clearance. A variety of other outcomes also must be considered in defining adequate therapy in ARF, including non–urea solute clearance, achieving volume control with minimal hemodynamic consequences, and maintenance of acid-base and electrolyte homeostasis. The ultimate definition of adequacy of RRT in ARF also must take into consideration its effects on mortality and recovery of renal function. Hence, many operational factors such as timing of initiation of RRT, mode of therapy, selection of membrane, and dose and duration of therapy all play a role in ensuring delivery of adequate dialysis to patients with ARF.[9] Although there is much data in the literature discussing these issues in the chronic renal failure setting, no current standards exist with regard to the practice of RRT for patients with ARF.[10,11] Current RRT practice principles for patients with ARF generally have been extrapolated from the ESRD literature, however, the application of these principles to ARF patients is fraught with numerous limitations. In this article we address some of these issues, with particular emphasis on the dose of dialysis as a surrogate to adequacy of dialysis in the ARF setting.

Measuring Adequacy of Dialysis in ARF

The measurement of dialysis adequacy in patients with ESRD generally involves the use of urea kinetic modeling. In patients with ARF, multiple methods of measuring adequacy of

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dialysis have been used including single-pool and double-pool urea kinetics and blood-based and dialysate-based urea kinetic modeling.[12] All of these methods have been extrapolated from ESRD literature. This extrapolation is problematic for several reasons. First, no consensus exists, even in ESRD patients, with regard to the preferred method of measuring adequacy of dialysis (eg, single-pool urea kinetics versus double-pool urea kinetics). Second, as discussed earlier, ARF differs significantly from ESRD in that there are very large differences in the catabolic rate and total body water content between these patient groups, and several operational factors such as vascular access and hemodynamic tolerance for intermittent hemodialysis (IHD) widely differ between the groups. Third, urea-kinetic modeling assumes a steady state in the body for urea, in which urea production equals urea removal.[13] Urea-kinetic modeling also assumes that the volume of distribution of urea is approximately equal to total body water, an assumption that does not hold in ARF.[14,15] Both of these assumptions clearly do not hold in the intensive care unit setting where most cases of ARF occur. In the case of pure hemofiltration, clearance and, hence, the dose generally is considered to be directly proportional to the ultrafiltration rate (mL/kg/h). However, once dialysate is added, this relationship no longer holds. In addition, comparing the dose equivalence of IHD and continuous renal replacement therapy (CRRT) has been difficult.[16]

Timing of Initiation of RRT in ARF

There is no consensus on the indications for RRT in patients with ARF. Similar to other aspects of RRT, the indications generally have been extrapolated from the ESRD experience. Although there is little dispute regarding the necessity of RRT for the treatment of refractory hyperkalemia, fluid overload refractory to diuretic therapy, severe metabolic acidosis, or overt uremic symptoms, there is no consensus on the degree of azotemia or on the duration of renal failure warranting initiation of therapy in the absence of these absolute indications. Intuitively, many would argue, the earlier an intervention is provided, the better the outcome will be. However, evidence in support of this notion in ARF is lacking. Many patients with ARF recover renal function without requiring any RRT. Excessively early initiation therefore poses the risk for initiating therapy in patients who might never require dialysis using a more conservative approach. On the other hand, early initiation in these patients still might have a beneficial outcome. ARF frequently occurs in the setting of multiple organ dysfunction syndrome, thus consideration of the impact of ARF on other failing organs must factor in the timing of RRT. Second, in ARF during critical illness, increased catabolism along with the continued need to administer adequate nutritional protein leads to increased urea generation. Third, volume intake in these patients cannot be limited, owing to the obligate administration of intravenous medications such as antibiotics and continuous infusions of vasopressors. Finally, these patients may be sensitive to metabolic derangements and swings in their acid-base and electrolyte status may be tolerated poorly. Hence, waiting for conventional indications for initiation of RRT in patients with ARF may be inappropriate. One retrospective study that used serum blood urea nitrogen (BUN) levels as a surrogate for timing of initiation of dialysis in ARF showed that patients who were dialyzed earlier in the course of their disease (mean BUN, 42.6 mg/dL) had a better survival (39% versus 20%) compared with those in whom dialysis was initiated later (mean BUN, 94.5 mg/dL).[17] Although the interpretation of this retrospective study is complicated by potentially different reasons for the initiation of RRT in the 2 groups, these data suggest that initiation of RRT earlier in the course of ARF may be of benefit. However, a recent study by Bouman et al,[18] does not support this finding (n = 106). In this study, patients were randomized to 3 groups: early high-volume hemofiltration (n = 35; 72-96 L/24 h), early low-volume hemofiltration (n = 35; 24-36 L/24 h), and late low-volume hemofiltration (n = 36; 24-36 L/24 h). In this study, survival at 28 days and recovery of renal function were not improved using early initiation of hemofiltration. This study was limited in that it clearly was underpowered to detect any differences in outcome.

Mode of Dialysis

There is no clear consensus as to which, if any, modality of RRT is superior with regard to improving clinical outcomes in ARF. Although peritoneal dialysis (PD) is continuous and uses a biocompatible membrane (peritoneal lining), the solute clearance and fluid removal rate often are dependent on peritoneal perfusion. The application of PD also may be limited by technical factors, an increased risk for infection, and hyperglycemia from the high glucose content of peritoneal dialysate. Hence, this mode has fallen into disfavor in the ARF setting. A recent randomized trial compared PD with continuous venovenous hemofiltration (CVVH) in patients with infection-associated ARF.[19] In this study, 70 adult patients with infection-associated ARF (severe falciparum malaria, n = 48; or sepsis, n = 22) were enrolled; 34 patients were assigned to CVVH and 36 patients were assigned to PD. The mortality rate was 47% (17 patients) in the group randomized to PD, as compared with 15% (5 patients) in the group assigned to CVVH ($P = .005$). The rates of resolution of acidosis and of a decrease in the serum creatinine concentration associated with CVVH were more than double those observed with PD ($P < .005$), and the duration of RRT was also significantly shorter in the patients randomized to CVVH.

The relative roles of IHD and CRRT in ARF remains debated. An ideal strategy of RRT should provide steady control of uremic solutes, extracellular volume, and electrolyte and acid-base balance while producing minimal hemodynamic disturbance. As the result of the more rapid solute and volume removal necessary with IHD, it is associated with a greater risk for hypotension than CRRT.[20-22] As a result, CRRT frequently is used preferentially in critically ill patients with hemodynamic instability. In addition, CRRT has a

greater efficiency for control of low molecular weight solutes than alternate-day IHD,[16,23-25] and eliminates the saw-tooth pattern of volume and solute control associated with IHD. However, despite these advantages of CRRT, evidence supporting its superiority over IHD with regard to mortality or other clinical outcome measures is lacking. Many studies have compared these 2 modalities but have provided conflicting results. Most of these studies have been limited by their observational nature or by large differences in baseline characteristics of the patient population. Two observational studies used multivariate analyses of ARF patients to evaluate the effect of the mode of dialysis on clinical outcome and found that the mode of dialysis did not impact clinical outcome.[26,27] Subsequently, a recent randomized controlled trial compared IHD with CRRT (N = 166) and showed increased intensive care unit and in-hospital mortality with CRRT compared with IHD.[28] This study, however, showed that recovery of renal function was better in survivors treated with CRRT than IHD. This study had several important limitations. In this study, despite randomization, there were significant differences between the groups in several covariates independently associated with mortality, including sex, hepatic failure, Acute Physiology and Chronic Health Evaluation (APACHE) II and III scores, and the number of failed organ systems, in each instance biased in favor of the IHD group. Also, several confounding factors such as the timing of initiation of dialysis and the dose of dialysis were not controlled for in this study. Although a recent meta-analysis showed that when adjusted for study quality and severity of illness, mortality was lower in patients treated with CRRT compared with IHD (relative risk, .72; (.60-.87); $P < .01$),[29] these results were contradicted by a second meta-analysis[30] that limited itself to randomized trials.

In summary, debate still exists as to whether CRRT is better than IHD in the setting of ARF. Although CRRT often is considered the modality of choice in patients with hemodynamic instability, this has not been shown rigorously. Similarly, although CRRT offers theoretic advantages even in patients without hemodynamic compromise, this view has not been validated clinically. A recent international consensus conference also concluded that because of the lack of evidence, no firm overall recommendations for patient selection for CRRT could be made, except in the setting of coexisting intracranial hypertension, in which CRRT appears to be superior.[11]

Dialysis Membranes

An ideal strategy of RRT not only should be able to provide timely and efficient support, but also has to provide it in a biocompatible manner. It has been shown that activation of complement and coagulation factors occurs during contact between blood and the dialysis membrane.[31-33] Neutrophil activation and sequestration occurs in the lungs and other organs as well. All of these factors contribute to the hemodynamic changes and hypersensitivity-like reactions during dialysis. This is especially apparent with cellulose-based membranes that activate the alternative pathway of complement both in vitro and in vivo.[34] Cellulose membranes can be classified broadly into unsubstituted (eg, cuprophane) membranes and substituted membranes, such as cellulose acetate and cellulose diacetate. In addition to the immunologic effects, exposure to cellulosic membranes has been shown to result in net protein catabolism.[35] The newer synthetic membranes, such as polyacrylonitrile, polymethyl methyl-acrylate, polyamide, and polysulfone have been shown to cause a lesser degree of activation of the inflammatory response, and again loosely have been dubbed as *biocompatible* membranes. Many studies have assessed the effect of biocompatibility on outcomes in patients undergoing dialysis for ARF and have reported inconsistent results. However, no single study has been of sufficient size to be definitive. In addition, 2 recent meta-analyses addressed this issue but found inconsistent results.[36,37] Although the first meta-analysis found insufficient evidence that membrane composition influenced hospital mortality, the second, which included a larger number of studies, concluded that cellulose membranes were associated with worse survival to hospital discharge compared with synthetic membranes. Thus, based on current literature, the general consensus is that synthetic membranes are associated with improved outcomes compared with unsubstituted cellulose membranes. Whether synthetic membranes are superior to substituted (modified) cellulose membranes (ie, cellulose triacetate, and so forth) still remains controversial.

Dose of Dialysis

In ESRD, increasing the dialysis dose, within limits, is associated with decreased morbidity and mortality.[6,38] The dose of dialysis commonly is quantified by using the unitless index, Kt/V, in which K represents urea clearance, t is the time of dialysis, and V is the volume of distribution of urea. The literature has supported a single-pool Kt/V urea of at least 1.2 per treatment as the minimum dose in patients with ESRD,[6,39] although higher doses were not supported by the recently published Hemodialysis (HEMO) study.[40] Although small, retrospective, and nonrandomized studies support the hypothesis that increasing the delivered dose of RRT is associated with improved survival in patients with ARF,[41,42] until recently this hypothesis had not been tested by any randomized trials. Although an optimal dialysis dose has not been established in patients with ARF,[43] it generally is accepted that the delivered dose of dialysis should be at least as great as that recommended for ESRD.[11]

Despite this, a recent prospective study of 40 patients (136 dialysis treatments) with ARF treated with IHD, reported that prescribed Kt/V was less than 1.2 in 49% of treatments and, more importantly, delivered Kt/V was less than 1.2 in nearly 70% of treatments.[44] Multiple factors can lead to discrepancies between the prescribed and delivered dose of dialysis in ARF, including catheter dysfunction leading to recirculation of dialyzed blood, inadequate anticoagulation resulting in clotting of the dialysis fibers, and decreases in actual dialysis time as a result of hemodynamic instability.

In a recent study, Schiffl et al[45] assigned 160 critically ill patients with severe ischemic or nephrotoxic acute tubular

necrosis to daily or every-other-day hemodialysis, in alternating order. Patients were excluded from the study if they had an indication for CRRT. The primary study end point was survival with duration of ARF and the frequency of therapy-related complications was evaluated as a secondary end point. The 2 study groups were similar at baseline. Mortality was 28% in patients assigned to daily IHD as compared with 46% with alternate-day dialysis ($P = .01$). Daily hemodialysis also resulted in more rapid resolution of ARF (mean [±SD], 9 ± 2 versus 16 ± 6 d; $P = .001$), better control of uremia, and fewer hypotensive episodes during hemodialysis than did conventional hemodialysis. Although this study is supportive of a more intensive dialysis prescription in ARF, there are many problems with the study's design and implementation. First, the exclusion of patients with an indication for CRRT eliminated the sickest patients and diminished the generalizability of the study. Second, the nonrandom assignment of patients to groups may have introduced bias, although the reported baseline characteristics of the 2 groups appear similar. Finally, the delivered dose of therapy in the alternate-day group was substantially lower than accepted adequate hemodialysis for chronic kidney disease, resulting in a mean predialysis BUN level of 104 mg/dL in this group and an increased incidence of uremic complications, including infection and gastrointestinal bleeding.

In CRRT, the dose of therapy correlates with the effluent flow rate.[46-48] In continuous hemofiltration, the sieving coefficients of low molecular weight solutes are approximately 1, resulting in equivalence between effluent flow rate and clearance. In continuous hemodialysis, solute equilibration also is almost complete, resulting in near equivalence between dialysate flow and clearance.[49] By using effluent flow as an index of the dose of therapy, in a recent single-center randomized controlled trial Ronco et al[50] showed that higher CVVH doses (35 mL/kg/h) improved patient survival in ARF compared with conventional doses (20 mL/kg/h), whereas further increases in dose to 45 mL/kg/h were not helpful. Survival was 41% in the 20-mL/kg/h group versus 57% in the 35-mL/kg/h group and 58% in the 45-mL/kg/h group ($P < .001$). Of note, more than 90% of patients in this study received the prescribed dialysis dose. However, a second recent randomized controlled trial did not show similar results. In this smaller study, 106 ventilated, severely ill patients with oliguric ARF were randomized to 3 groups.[18] Thirty-five patients were treated with early high-volume hemofiltration (72-96 L/24 h), 35 patients with early low-volume hemofiltration (24-36 L/24 h), and 36 patients with late low-volume hemofiltration (24-36 L/24 h). The median ultrafiltrate rate was 48.2 mL/kg/h (42.3-58.7 mL/kg/h) in the early high-volume hemofiltration, 20.1 mL/kg/h (17.5-22.0 mL/kg/h) in the early low-volume hemofiltration, and 19.0 mL/kg/h (16.6-21.1 mL/kg/h) in the late low-volume hemofiltration groups, respectively. No differences in 28-day survival or duration of ARF were found between these groups. Hence, this study concluded that in critically ill patients with oliguric ARF, survival at 28 days and recovery of renal function were not improved using high ultrafiltrate volumes or early initiation of hemofiltration. However, this study was limited in that it was underpowered and probably enrolled fewer sick patients as suggested by the very high survival rates in both the groups.

In addition, more importantly, CRRT delivery may not reach the levels prescribed. In a single-center retrospective review of CRRT dosing patterns, we found that the mean CRRT dose prescribed for patients with ARF was only 24.46 ± 6.73 mL/kg/h, and that the mean dose delivered was merely 16.55 ± 5.41 mL/kg/h (68% of the prescribed dose, $P < .000001$).[51] The average number of hours per day on CRRT was 16.1 ± 3.53 (mean ± SD), with a mean flow rate (averaged over 24 hours) of 1.36 ± 0.31 L/h. Although there was a high concordance between the prescribed and delivered effluent flow rates in this study, the treatment time was decreased owing to interruptions in therapy.

In summary, these clinical studies have suggested that more intensive renal support likely results in improved survival. These studies, however, have had significant limitations and have not been widely accepted into clinical practice. An ongoing multicenter trial is now comparing intensive renal support with conventional management of RRT in critically ill patients with ARF to provide a more definitive answer to this question.

Conclusion

Despite the use of RRT for patients with ARF over the past 3 decades, a clear understanding on how best to provide adequate dialysis is lacking. Adequate dialysis is defined poorly and involves multiple operational factors, each one of which might independently influence patient outcome. No current standard exists on how to define, measure, and deliver adequate dialysis accurately in the ARF setting. However, based on our current understanding, review of the existing literature, and physiologic reasoning, the following general recommendations can be made with regard to delivering adequate dialysis effectively. First, indications for RRT in ARF differ from that in ESRD, and patients with ARF may benefit from early initiation of RRT. Second, CRRT may be better tolerated than IHD in patients with hemodynamic instability, and although not clearly associated with improved survival, may be associated with greater recovery of renal function. Third, unsubstituted cellulose membrane–containing filters should be avoided. Finally, a Kt/V of at least 1.2 per treatment 3 times per week should be delivered in patients with ARF if IHD is used. Although the evidence is limited and debatable, until further evidence is available, we recommend that an ultrafiltration rate of 35 mL/kg/h be delivered if CRRT is the modality used.

References

1. Chertow GM, Christiansen CL, Cleary PD, et al: Prognostic stratification in critically ill patients with acute renal failure requiring dialysis. Arch Intern Med 155:1505-1511, 1995
2. Bellomo R, Ronco C: The changing pattern of severe acute renal failure. Nephrology 2:602-610, 1991
3. Hou SH, Bushinsky DA, Wish JB, et al: Hospital-acquired renal insufficiency: A prospective study. Am J Med 74:243-248, 1983
4. Liano F, Pascual J: Outcomes in acute renal failure. Semin Nephrol 18:541-550, 1998

5. Liano F, Junco E, Pascual J, et al: The spectrum of acute renal failure in the intensive care unit compared with that seen in other settings. The Madrid Acute Renal Failure Study Group. Kidney Int Suppl 66: S16-S24, 1998
6. National Kidney Foundation: NKF-DOQI clinical practice guidelines for hemodialysis adequacy. Am J Kidney Dis 30:15-66, 1997
7. Parker TF III, Husni L, Huang W, et al: Survival of hemodialysis patients in the United States is improved with a greater quantity of dialysis. Am J Kidney Dis 23:670-680, 1994
8. Lowrie EG, Li Z, Ofsthun N, et al: Body size, dialysis dose and death risk relationships among hemodialysis patients. Kidney Int 62:1891-1897, 2002
9. Bellomo R, Ronco C: Acute renal failure in the intensive care unit: Adequacy of dialysis and the case for continuous therapies. Nephrol Dial Transplant 11:424-428, 1996
10. Cole L, Bellomo R, Silvester W, et al: A prospective, multicenter study of the epidemiology, management, and outcome of severe acute renal failure in a "closed" ICU system. Am J Respir Crit Care Med 162:191-196, 2000
11. Kellum JA, Mehta RL, Angus DC, et al: The first international consensus conference on continuous renal replacement therapy. Kidney Int 62: 1855-1863, 2002
12. Friedman AN, Jaber BL: Dialysis adequacy in patients with acute renal failure. Curr Opin Nephrol Hypertens 8:695-700, 1999
13. Sargent JA: Control of dialysis by a single-pool urea model: the National Cooperative Dialysis Study. Kidney Int Suppl S19-S25, 1983
14. Himmelfarb J, Evanson J, Hakim RM, et al: Urea volume of distribution exceeds total body water in patients with acute renal failure. Kidney Int 61:317-323, 2002
15. Ikizler TA, Sezer MT, Flakoll PJ, et al: Urea space and total body water measurements by stable isotopes in patients with acute renal failure. Kidney Int 65:725-732, 2004
16. Liao Z, Zhang W, Hardy PA, et al: Kinetic comparison of different acute dialysis therapies. Artif Organs 27:802-807, 2003
17. Gettings LG, Reynolds HN, Scalea T: Outcome in post-traumatic acute renal failure when continuous renal replacement therapy is applied early vs. late. Intensive Care Med 25:805-813, 1999
18. Bouman CSC, Oudemans-van Straaten HM, Tijssen JGP: Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure. A prospective randomized trial. Crit Care Med 30:2205-2211, 2002
19. Phu NH, Hien TT, Mai NT, et al: Hemofiltration and peritoneal dialysis in infection-associated acute renal failure in Vietnam. N Engl J Med 347:895-902, 2002
20. Tisler A, Akocsi K, Borbas B, et al: The effect of frequent or occasional dialysis-associated hypotension on survival of patients on maintenance haemodialysis. Nephrol Dial Transplant 18:2601-2605, 2003
21. Maeda K, Shinzato T, Nakai S, et al: Mechanism of dialysis-induced hypotension. Nagoya J Med Sci 54:1-10, 1992
22. Servilla KS, Groggel GC: Anterior ischemic optic neuropathy as a complication of hemodialysis. Am J Kidney Dis 8:61-63, 1986
23. Clark WR, Mueller BA, Kraus MA, et al: Extracorporeal therapy requirements for patients with acute renal failure. J Am Soc Nephrol 8:804-812, 1997
24. Bellomo R, Parkin G, Love J, et al: Management of acute renal failure in the critically ill with continuous venovenous hemodiafiltration. Ren Fail 14:183-186, 1992
25. Clark WR, Mueller BA, Alaka KJ, et al: A comparison of metabolic control by continuous and intermittent therapies in acute renal failure. J Am Soc Nephrol 4:1413-1420, 1994
26. Guerin C, Girard R, Selli JM, et al: Intermittent versus continuous renal replacement therapy for acute renal failure in intensive care units: Results from a multicenter prospective epidemiological survey. Intensive Care Med 28:1411-1418, 2002
27. Swartz RD, Messana JM, Orzol S, et al: Comparing continuous hemofiltration with hemodialysis in patients with severe acute renal failure. Am J Kidney Dis 34:424-432, 1999
28. Mehta RL, McDonald B, Gabbai FB, et al: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int 60:1154-1163, 2001
29. Kellum JA, Angus DC, Johnson JP, et al: Continuous versus intermittent renal replacement therapy: A meta-analysis. Intensive Care Med 28:29-37, 2002
30. Tonelli M, Manns B, Feller-Kopman D: Acute renal failure in the intensive care unit: A systematic review of the impact of dialytic modality on mortality and renal recovery. Am J Kidney Dis 40:875-885, 2002
31. Craddock PR, Fehr J, Brigham KL, et al: Complement and leukocyte-mediated pulmonary dysfunction in hemodialysis. N Engl J Med 296: 769-774, 1977
32. Hakim RM, Schafer AI: Hemodialysis-associated platelet activation and thrombocytopenia. Am J Med 78:575-580, 1985
33. Schulman G, Hakim RM: Recent advances in the biocompatibility of haemodialysis membranes. Nephrol Dial Transplant 6:10-13, 1991 (suppl)
34. Chenoweth DE, Henderson LW: Complement activation during hemodialysis: Laboratory evaluation of hemodialyzers. Artif Organs 11:155-162, 1987
35. Bouffard Y, Viale JP, Annat G, et al: Energy expenditure in the acute renal failure patient mechanically ventilated. Intensive Care Med 13: 401-404, 1987
36. Jaber BL, Lau J, Schmid CH, et al: Effect of biocompatibility of hemodialysis membranes on mortality in acute renal failure: A meta-analysis. Clin Nephrol 57:274-282, 2002
37. Subramanian S, Venkataraman R, Kellum JA: Influence of dialysis membranes on outcomes in acute renal failure: A meta-analysis. Kidney Int 62:1819-1823, 2002
38. Wu AW, Fink NE, Cagney KA, et al: Developing a health-related quality-of-life measure for end-stage renal disease: The CHOICE Health Experience Questionnaire. Am J Kidney Dis 37:11-21, 2001
39. Owen WF Jr, Chertow GM, Lazarus JM, et al: Dose of hemodialysis and survival: Differences by race and sex. JAMA 280:1764-1768, 1998
40. Eknoyan G, Beck GJ, Cheung AK, et al: Effect of dialysis dose and membrane flux in maintenance hemodialysis. N Engl J Med 347:2010-2019, 2002
41. Paganini EP, Tapolyai M, Goormastic M, et al: Establishing a dialysis therapy/patient outcome link in intensive care unit acute dialysis for patients with acute renal failure. Am J Kidney Dis 28:S81-S89, 1996
42. Schiffl H, Lang S, Konig A, et al: Dose of intermittent hemodialysis and outcome of acute renal failure: A prospective randomized study. J Am Soc Nephrol 8:290A, 1997
43. Leblanc M, Tapolyai M, Paganini EP: What dialysis dose should be provided in acute renal failure? A review. Adv Ren Replace Ther 2:255-264, 1995
44. Evanson JA, Himmelfarb J, Wingard R, et al: Prescribed versus delivered dialysis in acute renal failure patients. Am J Kidney Dis 32:731-738, 1998
45. Schiffl H, Lang SM, Fischer R: Daily hemodialysis and the outcome of acute renal failure. N Engl J Med 346:305-310, 2002
46. Brunet S, Leblanc M, Geadah D, et al: Diffusive and convective solute clearances during continuous renal replacement therapy at various dialysate and ultrafiltration flow rates. Am J Kidney Dis 34:486-492, 1999
47. Clark WR, Murphy MH, Alaka KJ, et al: Urea kinetics during continuous hemofiltration. ASAIO J 38:664-667, 1992
48. Clark WR, Turk JE, Kraus MA, et al: Dose determinants in continuous renal replacement therapy. Artif Organs 27:815-820, 2003
49. Clark WR, Ronco C: Renal replacement therapy in acute renal failure: Solute removal mechanisms and dose quantification. Kidney Int Suppl 66:S133-S137, 1998
50. Ronco C, Bellomo R, Homel P, et al: Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: A prospective randomised trial. Lancet 356:26-30, 2000
51. Venkataraman R, Kellum JA, Palevsky P: Dosing patterns for continuous renal replacement therapy at a large academic medical center in the United States. J Crit Care 17:246-250, 2002