Selection of Modality of Renal Replacement Therapy

Tania Abi Antoun* and Paul M. Palevsky*†
*Renal-Electrolyte Division, University of Pittsburgh School of Medicine and †The Renal Section, VA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania

ABSTRACT

The proliferation of new technologies has led to the availability of a broad range of options for the management of renal replacement therapy (RRT) in patients with acute kidney injury. We provide a review of the published literature comparing the continuous RRTs (CRRT) with other modalities of renal support, including intermittent hemodialysis and the more recently described "hybrid" therapies such as sustained, low efficiency dialysis as well as compare arteriovenous and venovenous and convective and diffusive modalities of CRRT. While there is clear evidence that venovenous therapies are superior to arteriovenous therapies, current evidence does not support superiority of convective when compared with diffusive therapies or greater survival or recovery of kidney function with any individual modality of RRT. Selection of modality of RRT should therefore rely on the resources and expertise available.

Acute kidney injury (AKI) afflicts 20–30% of patients admitted to the intensive care unit (ICU) and is associated with substantial added morbidity and mortality (1–3). Patients with AKI requiring renal replacement have mortality rates in excess of 50% (1,4–6), a prognosis that has remained stable over several decades despite multiple advances in the practice of critical care medicine and nephrology. In addition to uncertainty regarding the optimal timing of initiation of renal replacement therapy (RRT), the proliferation of modalities of RRT over the past three decades has provided nephrologists and intensivists with an increasing selection of options for managing renal support. RRT can be provided as hemodialysis, hemofiltration, or a combination thereof and as short intermittent treatments, continuous therapy or, more recently, as more prolonged, but intermittent, treatments. The medical literature is brimming with studies designed to demonstrate superiority of one regimen over the others, but few questions have been answered thus far. It remains incumbent on the provider to sieve through the available data to decide on the modality of RRT to use in an individual critically ill patient.

Address correspondence to: Paul M. Palevsky, MD, Room 7E123 (111F-U), VA Pittsburgh Healthcare System, University Drive, Pittsburgh, PA 15240, or e-mail: palevsky@pitt.edu.

Seminars in Dialysis—Vol 22, No 2 (March–April) 2009 pp. 108–113
DOI: 10.1111/j.1525-139X.2008.00540.x
© 2009 Wiley Periodicals, Inc.

Comparison of CRRT with Other Modalities of Renal Replacement Therapy

Comparison with Intermittent Hemodialysis

Since their initial description in 1977 (7), the continuous RRTs (CRRT) have gained wide application in intensive care units (ICUs), often supplanting intermittent hemodialysis (IHD) because of the belief that CRRT provides more efficient solute clearance, more sustained correction of electrolyte disturbances, and allows for better volume management. Advocates of CRRT also contend that it is better tolerated in hemodynamically unstable patients, making it their modality of choice in the critically ill. However, the evidence in support of this view is somewhat tenuous, with the validity of many supporting studies limited by nonrandomized or retrospective designs (Table 1) (8–24).

Unadjusted analyses have suggested that patients treated with CRRT have worse survival than those who receive IHD, an observation which may be explained by a greater disease burden in patients who are treated with CRRT when compared with IHD. In an attempt to eliminate this bias, Swartz et al. (18) performed a retrospective outcome analysis of 349 patients with AKI requiring renal replacement at the University of Michigan Medical Center between 1995 and 1996. Whereas initial univariate analysis showed that odds of death for initial treatment with continuous venovenous hemofiltration (CVVH) was greater than 2.03 when compared with IHD ($p < 0.01$), adjustment for greater severity of illness using a multivariate model provided an adjusted odds of death among patients assigned to initial CVVH

TABLE 1. Studies comparing CRRT and IHD

Study	RCT	Number of IHD patients	Number of CRRT patients	IHD mortality (%)	CRRT mortality (%)	Odds of death with IHD (95% confidence interval)	Risk adjusted odds/risk of death with IHD (95% confidence interval)
Mauritz et al. (8)	No	22	36	91	75	3.3	NR
Paganini et al. (9)	No	47	27	81	82	1.0	NR
McDonald et al. (10)	No	10	22	70	82	0.5	NR
Kierdorf et al. (11)	No	73	73	93	78	3.8	NR
Bastien et al. (12)	No	32	34	75	50	3.0	NR
Kruczynski et al. (13)	No	23	12	83	33	9.5	NR
Bellomo et al. (14)	No	84	150	70	61	1.5	NR
van Bommel et al. (15)	No	34	60	41	57	0.5	NR
Rialp et al. (16)	No	21	43	67	76	0.6	NR
Neveu et al. (17)	No	141	28	58	89	0.2	NR
Swartz et al. (18)	No	137	90	41	68	0.3	Not significant
Bellomo et al. (19)	No	47	47	70	53	1.2	NR
Mehta et al. (26)	Yes	82	84	48	66		0.63 (0.3–1.4)
John et al. (52)	Yes	20	10	70	70	1.0 (0.1–6.6)	
Ji et al. (20)	No	92	101	36	41	0.8	NR
Guerin et al. (21)	No	233	354	59	79	0.4	Not significant
Chang et al. (22)	No	95	53	54	79	0.3	NR
Augustine et al. (27)	Yes	40	40	70	68	1.12 (0.43–3.2)	
Gangji et al. (23)	No	66	36	58	64	0.8	Not significant
Swartz et al. (24)	No	183	200	40	65	0.4	Not significant
Uehlinger et al. (28)	Yes	55	70	51	47	1.16 (0.5–2.5)	
Vinsonneau et al. (29)	Yes	184	175	68	67	1.05 (0.6–1.7)	

NR, not reported; CRRT, continuous renal replacement therapies; IHD, intermittent hemodialysis; RCT, randomized controlled trials.

comparable to patients receiving initial IHD (1.09, $p = 0.72$). Although suggesting that the poor outcomes associated with CRRT can be ascribed to the underlying condition that prompted triage to CRRT and not the treatment modality itself, this analysis fails to support any intrinsic advantage of CVVH over IHD. Similar analyses by Guerin et al. (21) also demonstrated that the increased mortality associated with CRRT could be explained by the increased disease severity associated with its selection.

Five randomized controlled trials (RCTs) comparing IHD and CRRT have been published in peer-reviewed journals. One small RCT compared the effects of CVVH and IHD on systemic hemodynamics and splanchnic regional perfusion in septic patients with AKI (25). Thirty patients with similar baseline characteristics were assigned to CVVH ($n = 20$) or IHD ($n = 10$). After 24 hours of therapy and despite CVVH causing an increase in systemic vascular resistance and a decrease in cardiac output, no differences were found in intramucosal pCO_2 and pH, surrogate markers of splanchnic perfusion, suggesting that CVVH does not improve tissue oxygenation and mortality in septic patients with AKI. Although not the primary study endpoint, ICU mortality was the same (70%) in both treatment groups.

In the first multicenter RCT designed to assess the impact of modality of RRT on outcomes in AKI, Mehta et al. (26) randomized 166 critically ill adults with AKI to IHD or CRRT [continuous arteriovenous hemodiafiltration in 15.5% and continuous venovenous hemodiafiltration (CVVHDF) in 84.5%], excluding patients with hemodynamic instability, defined as a mean arterial pressure less than 70 mmHg. In the intention-to-treat analysis, mortality was greater in the CRRT group when compared with IHD group (28-day all-cause and ICU mortality: 59.5% versus 41.5%, $p = 0.02$); in-hospital mortality: 65.5% versus 47.6%, $p = 0.02$). Despite randomization, patients assigned to CRRT had higher APACHE (acute physiology and chronic health evaluation) III scores and more organ system failures and a greater proportion had liver failure, all of which were independently associated with mortality. After adjustment for these unbalanced covariates, the odds of death associated with CRRT was 1.58 (95% confidence interval 0.7–3.3), suggesting that baseline severity of disease accounted for the difference in mortality between CRRT and IHD. Complete renal recovery in survivors was more likely in patients who received CRRT and was also strongly influenced by the APACHE scores. In addition to the issues associated with imbalanced randomization, interpretation of this study is additionally confounded by a high rate of crossover between treatment modalities in both study arms.

A single center randomized prospective trial conducted at the Cleveland Clinic compared continuous and intermittent RRT in 80 patients assigned to either continuous venovenous hemodialysis (CVVHD) or IHD after matching for baseline illness severity (27). Although this study found some differences with respect to greater fluid removal and decreased vasopressor requirement in patients assigned to CVVHD, mortality was similar in CVVHD and IHD arms (67.5% versus 70% respectively, $p > 0.99$) as was the rate of kidney recovery.

In another single-center study, Uehlinger et al. (28) randomized 125 patients with AKI admitted to an ICU at a university hospital in Switzerland between 1998 and

2000 to CVVHDF ($n = 70$) or IHD ($n = 55$). The two groups were comparable at initiation of therapy with respect to gender, severity of illness, etiology, and markers of AKI. No differences were found in ICU mortality (34% CVVHDF versus 38% IHD, OR 1.16, $p = 0.71$) or in-hospital mortality (47% CVVHD versus 51% IHD, OR 1.18, $p = 0.72$). There was also no difference in hemodynamic stability, use of vasopressor agents, fluid balance, duration of RRT, recovery of kidney function, or length of stay. Of note, to avoid inciting or exacerbating hemodynamic instability, IHD was provided using short (2–3 hours) treatments with limited ultrafiltration during the first days of therapy, resulting in a requirement for daily IHD sessions for the majority of patients. Over the duration of treatment, the median frequency of IHD was 5 sessions/week.

More recently, the results of the Hemodiafe Study, the largest prospective randomized controlled study comparing CRRT and IHD have been reported (29). This study enrolled 360 patients in 21 ICUs in France between 1999 and 2003. Among the 359 patients who received their assigned treatment (IHD: $n = 184$; CVVHDF: $n = 175$; one patient randomized to CVVHDF withdrew consent prior to treatment) there was no difference in the primary study endpoint of 60-day survival between treatment groups (31.5% in IHD versus 32.6% in CVVHDF; $p = 0.98$). Treatment modality also had no significant effect on length of stay, rate, and time to recovery of kidney function or frequency of adverse events (except for hypothermia which was more common during CVVHDF). Interestingly, despite the hemodynamically unstable population (vasopressors were used in greater than 85% of patients), IHD was not associated with increased frequency of hypotension, a finding the Hemodiafe study group ascribed to standardized use of synthetic membranes, bicarbonate buffers and adherence to strict guidelines including gradual ultrafiltration, and use of cool dialysate with a high sodium concentration. This led the investigators to conclude that virtually all patients can be treated with IHD under standardized conditions.

Multiple meta-analyses comparing outcomes with IHD and CRRT have been published. A 2002 meta-analysis by Kellum et al. (30) that included 13 studies (of which only three were RCTs) suggested that CRRT might be associated with a lower relative mortality risk after adjustment for severity of illness and study quality. In contrast, Tonelli et al. (31) concluded that CRRT does not seem to offer any survival advantage over IHD, restricting their meta-analysis to RCTs. Three more recent meta-analyses reached the same conclusion after including the RCTs by Uehlinger et al. and the Hemodiafe study group. A Cochrane review in 2007 analyzed 15 RCTs and found that mortality, renal recovery, and episodes of hypotension did not differ between modalities although mean arterial pressures were higher in patients on CRRT (32). A meta-analysis by Bagshaw et al. (33) included nine RCTs and again showed no differences in mortality or recovery of kidney function, although CRRT was associated with less hemodynamic instability and greater volume removal. The authors raised concern, however, that multiple flaws in design, conduct, and quality of the included studies prevented them from drawing any definitive conclusions about the effect of modality on outcome. Finally, a systematic review by Pannu et al. (34) examined data from 30 RCTs and eight prospective cohort studies, and found no differences in survival, hypotension, or recovery of kidney function in patients treated using CRRT when compared with IHD. However, they calculated greater costs associated with CRRT and therefore concluded that IHD may be preferable to CRRT in AKI patients.

Comparison with Hybrid Therapies

Sustained, low efficiency dialysis (SLED) and extended daily dialysis (EDD) are modified forms of IHD, sometimes referred to as hybrid therapies, devised to utilize standard IHD machine technology while providing the slower solute and fluid removal of CRRT. In these modalities, solute clearance and volume removal are extended over 6–16 hours using conventional hemodialysis machines with dialysate and blood flows that are intermediate between IHD and CRRT. Observational prospective studies have shown that SLED is safe and an effective method of treating AKI in critically ill patients with decreased cost when compared with CRRT (35). Although no studies have evaluated outcomes with these modalities, several studies have evaluated intermediate parameters. Keilstein et al. (35) randomized 39 patients to 12 hours of EDD or CVVH and observed no difference in efficiency or hemodynamic tolerability. In a second study, Kumar et al. (36) assigned 54 patients with AKI to either CRRT or EDD. EDD was found to be a safe and effective alternative to CRRT with comparable hemodynamic and solute clearance profile but with decreased incidence of clotting and lower anticoagulation requirements.

Comparison of Arteriovenous and Venovenous Therapies

Continuous renal replacement therapies were historically delivered via an arteriovenous circuit (7,37–39). Reliance on systemic pressure to drive blood flow through the extracorporeal circuit permitted the use of a technologically simple device extracorporeal circuit but imposed important limitations on achievable effective solute clearance. This was particularly problematic in the critically ill patient with hemodynamic instability in whom low systemic arterial pressure limited blood flow. In addition, the prolonged arterial cannulation required was associated with high rates of complications, including bleeding and arterial thrombosis (40).

As a result of the problems with the arteriovenous approach, venovenous modalities of the continuous therapies were developed (41–43). Using a single dual-lumen venous catheter for access, the venovenous modalities require a blood pump to provide a constant blood flow independent of mean arterial blood pressure. However, the use of a pump-driven extracorporeal circuit necessitates more sophisticated instrumentation, including pressure monitors and air-leak detectors. With

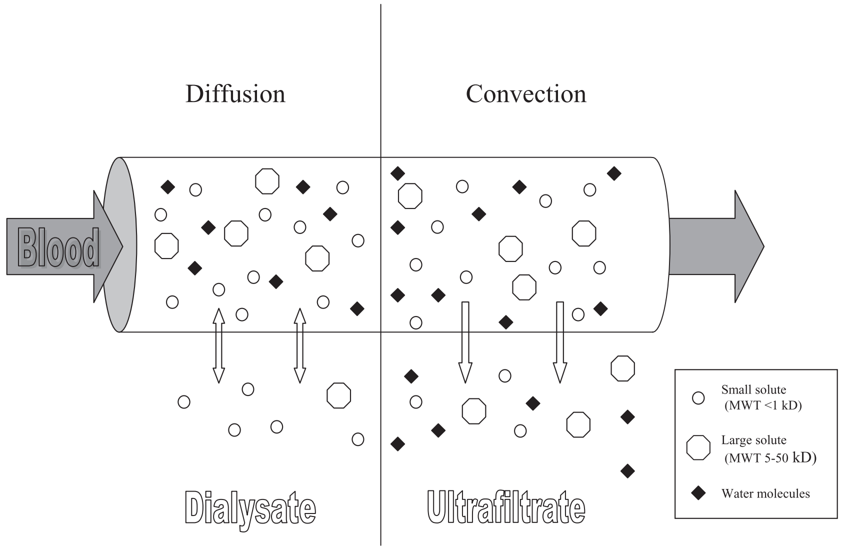

Fig. 1. Mechanisms of solute transport by diffusion (hemodialysis) and convection (hemofiltration). During hemodialysis, solutes diffuse down their concentration gradient from blood into dialysate. Solute removal for low molecular weight solutes is more efficient than for higher molecular weight solutes. During hemofiltration, solutes are transported entrained in the flow of plasma water during ultrafiltration (solvent drag) and passively cross the membrane in the absence of a concentration gradient. Solute removal for low and high molecular weight solutes is similar until the solute diameter approaches the membrane pore size.

the addition of balancing mechanisms for ultrafiltration control, the technological simplicity of continuous arteriovenous hemofiltration has been replaced by equipment that approaches the complexity of conventional hemodialysis machines. Given the more efficient solute clearance, more precise regulation of ultrafiltration and avoidance of prolonged arterial cannulation, with its potential complications of arterial injury, thrombosis and hemorrhage, the venovenous modalities of CRRT have virtually replaced the arteriovenous therapies (44). An expert consensus conference held in 2000 concluded that pump-driven venovenous therapy is the preferred modality for CRRT whenever the needed equipment and expertise for its implementation are available (45).

Comparison of Convective and Diffusive Therapies

Continuous therapy can be provided as hemofiltration, hemodialysis, or hemodiafiltration. Continuous hemofiltration relies on convective solute clearance, whereas continuous dialysis provides primarily diffusive clearance (Fig. 1). Hemodiafiltration employs a variable combination of both mechanisms. Convection provides better clearance of middle molecules or solutes with molecular weights above 500–1000 Da. It was proposed that convective modalities (continuous hemofiltration and hemodiafiltration) modulate the immune response by clearing the cytokines that promote and perpetuate the systemic inflammatory response syndrome (SIRS) (46,47). Indeed, CVVH was associated with lower levels of plasma tumor necrosis factor-α (TNF-α) when compared with CVVHD in patients with severe AKI and SIRS, but other cytokine levels, including interleukin (IL)-6 and IL-10, were not affected (48). In trauma patients with multiple organ dysfunction but without renal failure, CVVH improves hemodynamics and respiratory parameters (49) and decreases TNF-α and IL-6 levels, although not to a significant extent (9). It has been argued, however, that cytokine clearance during hemofiltration is inconsequential in comparison to their endogenous production and that anti-inflammatory and pro-inflammatory cytokines are both removed by hemofiltration (50). In addition, membrane adsorption has contributes substantially to cytokine removal during CVVH, particularly when polyacrilonitrile membranes are used, and that saturation occurs rapidly, within the first 1–2 hours (51). Thus, in the absence of outcome data, no recommendations can be made to favor either convective or diffusive modalities.

Conclusions

The available evidence does not support any robust recommendations regarding the choice of RRT in the ICU. Continuous therapies may not offer a convincing survival advantage but have not been shown to be inferior therapy to IHD, either. With the wide availability of CRRT machines and the increasing complexity of critically ill patients, it is likely to remain one of the preferred modalities of renal replacement in the ICU. This is especially true in certain categories of patients, such as those with fulminant liver failure. The use of new hybrid modalities, such as SLED, is increasing as more centers develop familiarity with this technique. SLED may also serve as a bridging modality, as patients are transitioned from CRRT to conventional IHD. As no single modality has emerged as the standard of care, choosing a renal replacement strategy for the critically ill patient relies primarily on the resources available and personal expertise in any given institution. Future focus should be directed towards optimizing the currently available modalities, improving the safety and effectiveness of their use to improve the survival of patients with the ominous prognosis associated with AKI.

References

1. Liano F, Junco E, Pascual J, Madero R, Verde E: 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
2. Ostermann M, Chang RW: Acute kidney injury in the intensive care unit according to RIFLE. *Crit Care Med* 35: 1837–1843, 2007; quiz 1852.
3. Bagshaw SM, George C, Dinu I, Bellomo R: A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. *Nephrol Dial Transplant* 23:1203–1210, 2008
4. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C: Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 294:813–818, 2005
5. Star RA: Treatment of acute renal failure. *Kidney Int* 54:1817–1831, 1998
6. Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E, Schein RM, Smith MW, Swanson KM, Thompson BT, Vijayan A, Watnick S, Star RA, Peduzzi P: Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med* 359:7–20, 2008
7. Kramer P, Wigger W, Rieger J, Matthaei D, Scheler F: Arteriovenous haemofiltration: a new and simple method for treatment of overhydrated patients resistant to diuretics. *Klinische Wochenschrift* 55:1121–1122, 1977
8. Mauritz W, Sporn P, Schindler I, Zadrobilek E, Roth E, Appel W: Acute renal failure in abdominal infection. Comparison of hemodialysis and continuous arteriovenous hemofiltration. *Anasth Intensivther Notfallmed*. 21:212–217, 1986
9. Paganini EP: Slow continuous hemofiltration and slow continuous ultrafiltration. *ASAIO Trans* 34:63–66, 1988
10. McDonald BR, Mehta RL: Decreased mortality in patients with acute renal failure undergoing continuous arteriovenous hemodialysis. *Contrib Nephrol* 93:51–56, 1991
11. Kierdorf H: Continuous versus intermittent treatment: clinical results in acute renal failure. *Contrib Nephrol* 93:1–12, 1991
12. Bastien O, Saroul C, Hercule C, George M, Estanove S: Continuous venovenous hemodialysis after cardiac surgery. *Contrib Nephrol* 93:76–78, 1991
13. Kruczynski K, Irvine-Bird K, Toffelmire EB, Morton AR: A comparison of continuous arteriovenous hemofiltration and intermittent hemodialysis in acute renal failure patients in the intensive care unit. *ASAIO J* 39:M778–M781, 1993
14. Bellomo R, Farmer M, Parkin G, Wright C, Boyce N: Severe acute renal failure: a comparison of acute continuous hemodiafiltration and conventional dialytic therapy. *Nephron* 71:59–64, 1995
15. van Bommel E, Bouvy ND, So KL, Zietse R, Vincent HH, Bruining HA, Weimar W: Acute dialytic support for the critically ill: intermittent hemodialysis versus continuous arteriovenous hemodiafiltration. *Am J Nephrol* 15:192–200, 1995
16. Rialp G, Roglan A, Betbese AJ, Perez-Marquez M, Ballus J, Lopez-Velarde G, Santos JA, Bak E, Net A: Prognostic indexes and mortality in critically ill patients with acute renal failure treated with different dialytic techniques. *Ren Fail* 18:667–675, 1996
17. Neveu H, Kleinknecht D, Brivet F, Loirat P, Landais P: Prognostic factors in acute renal failure due to sepsis. Results of a prospective multicentre study. The French Study Group on Acute Renal Failure. *Nephrol Dial Transplant* 11:293–299, 1996
18. Swartz RD, Messana JM, Orzol S, Port FK: Comparing continuous hemofiltration with hemodialysis in patients with severe acute renal failure. *Am J Kidney Dis* 34:424–432, 1999
19. Bellomo R, Farmer M, Bhonagiri S, Porceddu S, Ariens M, M'Pisi D, Ronco C: Changing acute renal failure treatment from intermittent hemodialysis to continuous hemofiltration: impact on azotemic control. *Int J Artif Organs* 22:145–150, 1999
20. Ji D, Gong D, Xie H, Xu B, Liu Y, Li L: A retrospective study of continuous renal replacement therapy versus intermittent hemodialysis in severe acute renal failure. *Chin Med J (Engl)* 114:1157–1161, 2001
21. Guerin C, Girard R, Selli JM, Ayzac L: 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
22. Chang JW, Yang WS, Seo JW, Lee JS, Lee SK, Park SK: Continuous venovenous hemodiafiltration versus hemodialysis as renal replacement therapy in patients with acute renal failure in the intensive care unit. *Scand J Urol Nephrol* 38:417–421, 2004
23. Gangji AS, Rabbat CG, Margetts PJ: Benefit of continuous renal replacement therapy in subgroups of acutely ill patients: a retrospective analysis. *Clin Nephrol* 63:267–275, 2005
24. Swartz RD, Bustami RT, Daley JM, Gillespie BW, Port FK: Estimating the impact of renal replacement therapy choice on outcome in severe acute renal failure. *Clin Nephrol* 63:335–345, 2005
25. Holloway P, Benham S, St John A: The value of blood lactate measurements in ICU: an evaluation of the role in the management of patients on haemofiltration. *Clin Chim Acta* 307:9–13, 2001
26. Mehta RL, McDonald B, Gabbai FB, Pahl M, Pascual MT, Farkas A, Kaplan RM: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. *Kidney Int* 60:1154–1163, 2001
27. Augustine JJ, Sandy D, Seifert TH, Paganini EP: A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. *Am J Kidney Dis* 44:1000–1007, 2004
28. Uehlinger DE, Jakob SM, Ferrari P, Eichelberger M, Huynh-Do U, Marti HP, Mohaupt MG, Vogt B, Rothen HU, Regli B, Takala J, Frey FJ: Comparison of continuous and intermittent renal replacement therapy for acute renal failure. *Nephrol Dial Transplant* 20:1630–1637, 2005
29. Vinsonneau C, Camus C, Combes A, Costa de Beauregard MA, Klouche K, Boulain T, Pallot JL, Chiche JD, Taupin P, Landais P, Dhainaut JF: Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. *Lancet* 368:379–385, 2006
30. Kellum JA, Angus DC, Johnson JP, Leblanc M, Griffin M, Ramakrishnan N, Linde-Zwirble WT: Continuous versus intermittent renal replacement therapy: a meta-analysis. *Intensive Care Med* 28:29–37, 2002
31. 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
32. Rabindranath K, Adams J, Macleod AM, Muirhead N: Intermittent versus continuous renal replacement therapy for acute renal failure in adults. *Cochrane Database Syst Rev*:CD003773, 2007.
33. Bagshaw SM, Berthiaume LR, Delaney A, Bellomo R: Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: a meta-analysis. *Crit Care Med* 36:610–617, 2008
34. Pannu N, Klarenbach S, Wiebe N, Manns B, Tonelli M: Renal replacement therapy in patients with acute renal failure: a systematic review. *JAMA* 299:793–805, 2008
35. Kielstein JT, Kretschmer U, Ernst T, Hafer C, Bahr MJ, Haller H, Fliser D: Efficacy and cardiovascular tolerability of extended dialysis in critically ill patients: a randomized controlled study. *Am J Kidney Dis* 43:342–349, 2004
36. Kumar VA, Yeun JY, Depner TA, Don BR: Extended daily dialysis vs. continuous hemodialysis for ICU patients with acute renal failure: a two-year single center report. *Int J Artif Organs* 27:371–379, 2004
37. Paganini EP, Nakamoto S: Continuous slow ultrafiltration in oliguric acute renal failure. *Trans Am Soc Artif Intern Organs* 26:201–204, 1980
38. Lauer A, Saccaggi A, Ronco C, Belledonne M, Glabman S, Bosch JP: Continuous arteriovenous hemofiltration in the critically ill patient. Clinical use and operational characteristics. *Ann Intern Med* 99:455–460, 1983
39. Sigler MH, Teehan BP: Solute transport in continuous hemodialysis: a new treatment for acute renal failure. *Kidney Int* 32:562–571, 1987
40. Bellomo R, Parkin G, Love J, Boyce N: A prospective comparative study of continuous arteriovenous hemodiafiltration and continuous venovenous hemodiafiltration in critically ill patients. *Am J Kidney Dis* 21:400–404, 1993
41. Macias WL, Mueller BA, Scarim SK, Robinson M, Rudy DW: Continuous venovenous hemofiltration: an alternative to continuous arteriovenous hemofiltration and hemodiafiltration in acute renal failure. *Am J Kidney Dis* 18:451–458, 1991
42. Canaud B, Garred LJ, Christol JP, Aubas S, Beraud JJ, Mion C: Pump assisted continuous venovenous hemofiltration for treating acute uremia. *Kidney Int Suppl* 24:S154–S156, 1988
43. Wendon J, Smithies M, Sheppard M, Bullen K, Tinker J, Bihari D: Continuous high volume venous-venous haemofiltration in acute renal failure. *Intensive Care Med* 15:358–363, 1989
44. Overberger P, Pesacreta M, Palevsky PM: Management of renal replacement therapy in acute kidney injury: a survey of practitioner prescribing practices. *Clin J Am Soc Nephrol* 2:623–630, 2007
45. Kellum JA, Mehta RL, Angus DC, Palevsky P, Ronco C: The first international consensus conference on continuous renal replacement therapy. *Kidney Int* 62:1855–1863, 2002
46. Hoffmann JN, Hartl WH, Deppisch R, Faist E, Jochum M, Inthorn D: Hemofiltration in human sepsis: evidence for elimination of immunomodulatory substances. *Kidney Int* 48:1563–1570, 1995

47. Ronco C, Tetta C, Mariano F, Wratten ML, Bonello M, Bordoni V, Cardona X, Inguaggiato P, Pilotto L, d'Intini V, Bellomo R: Interpreting the mechanisms of continuous renal replacement therapy in sepsis: the peak concentration hypothesis. *Artif Organs* 27:792–801, 2003
48. Kellum JA, Johnson JP, Kramer D, Palevsky P, Brady JJ, Pinsky MR: Diffusive vs. convective therapy: effects on mediators of inflammation in patient with severe systemic inflammatory response syndrome. *Crit Care Med* 26:1995–2000, 1998
49. Sanchez-Izquierdo JA, Perez Vela JL, Lozano Quintana MJ, Alted Lopez E, Ortuno de Solo B, Ambros Checa A: Cytokines clearance during venovenous hemofiltration in the trauma patient. *Am J Kidney Dis* 30:483–488, 1997
50. Sieberth H, Kierdorf H: Is cytokine removal by continuous hemofiltration feasible? *Kidney Int* 56 (Suppl 72):S79–S83, 1999
51. De Vriese AS, Colardyn FA, Philippe JJ, Vanholder RC, De Sutter JH, Lameire NH: Cytokine removal during continuous hemofiltration in septic patients. *J Am Soc Nephrol* 10:846–853, 1999
52. John S, Griesbach D, Baumgartel M, Weihprecht H, Schmieder RE, Geiger H: Effects of continuous haemofiltration vs intermittent haemodialysis on systemic haemodynamics and splanchnic regional perfusion in septic shock patients: a prospective, randomized clinical trial. *Nephrol Dial Transplant* 16:320–327, 2001