A Comparison of Continuous Renal Replacement Therapy to Intermittent Dialysis in the Management of Renal Insufficiency in the Acutely Ill Surgical Patient

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Acute renal failure (ARF) occurs in 10 per cent to 23 per cent of intensive care unit patients with mortality ranging from 50 per cent to 90 per cent. ARF is characterized by an acute decline in renal function as measured by urine output (UOP), serum creatinine, and blood urea nitrogen (BUN). Causes may be prerenal, intrarenal, or postrenal. Treatment consists of renal replacement therapy (RRT), either intermittent (ID) or continuous (CRRT). Indications for initiation of dialysis include oliguria, acidemia, azotemia, hyperkalemia, uremic complications, or significant edema. Overall, the literature comparing CRRT to ID is poor. No studies of only surgical/trauma patients have been published. We hypothesize that renal function and hemodynamic stability in trauma/surgical critical care patients are better preserved by CRRT than by ID. We performed a retrospective review of trauma/surgical critical care patients requiring renal supportive therapy. Thirty patients received CRRT and 27 patients received ID. The study was controlled for severity of illness and demographics. Outcomes assessed were survival, renal function, acid-base balance, hemodynamic stability, and oxygenation/ventilation parameters. Populations were similar across demographics and severity of illness. Renal function, measured by creatinine clearance, was statistically greater with CRRT ($P = 0.035$). There was better control of azotemia with CRRT: BUN was lower ($P = 0.000$) and creatinine was lower ($P = 0.000$). Mean arterial blood pressure was greater ($P = 0.021$) with CRRT. No difference in oxygenation/ventilation parameters or pH was found between groups. CRRT results in an enhancement of renal function with improved creatinine clearance at the time of dialysis discontinuation. CRRT provides better control of azotemia while preserving hemodynamic stability in patients undergoing renal replacement therapy. Prospective randomized controlled studies and larger sample sizes are needed to further evaluate these modalities.

ACUTE RENAL FAILURE (ARF) occurs in 5–7 per cent of all hospitalized patients and in 10–23 per cent of patients admitted to the intensive care unit.[1, 2] Fifty to 70 per cent of ICU patients with ARF will require renal replacement therapy (RRT).[2] The mortality rate for all patients requiring RRT ranges from 40 per cent to 50 per cent.[1] For ICU patients requiring RRT, the mortality rate ranges from 50 per cent to 90 per cent.[2] Also for these patients in the ICU who survive, 5–30 per cent will require long-term hemodialysis (HD) without renal recovery.[3] ARF is characterized by an abrupt decline in renal function: an increase in serum creatinine by 0.5 mg/dL if the baseline was less than 2.5 mg/dL, or an increase of 20 per cent if baseline is greater than 2.5 mg/dL.[1]

There are no standards regarding the timing for initiation of RRT. Many nephrologists delay initiation due to concerns with hypotension, arrhythmias, and vascular access.[4] The delay in initiation of RRT may lead to prolonged time to recovery of renal function. Critically ill patients with ARF often have multiple organ dysfunction and could benefit from early initiation of RRT to decrease volume excess and aid in oxygenation and ventilation.[5] General indications for

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initiation of RRT include solute excess (hyperkalemia, azotemia), volume excess, or a combination of both.

Continuous RRT (CRRT) was first described in 1977 by Kramer for diuretic unresponsive fluid overload.[6] There are four basic types of CRRT: 1) slow continuous ultrafiltration (SCUF); 2) continuous venovenous hemofiltration (CVVH); 3) continuous venovenous hemodialysis (CVVHD); and 4) continuous venovenous hemodiafiltration (CVVHDF). CVVHDF is the most common modality. Blood is driven by a pump through a membrane, there is a slow countercurrent dialysate flow, and ultrafiltrate is removed and replacement fluids are often necessary. The process is both diffusive and convective. This modality allows for lower blood and dialysate flow rates, resulting in more hemodynamic stability. Significant fluid removal of 1 L/h is possible and volume may quickly be added if necessary. CRRT is unique in that solute removal is dissociated from fluid removal.[4] Time is not a limiting factor with CRRT. Other advantages of CRRT over intermittent dialysis (ID) are numerous and include the following: improved hemodynamic stability and better control of fluid and electrolyte shifts[4, 7, 8] and more efficient removal of middle and large molecular weight molecules such as cytokines due to convection.[4] Fluid balance can be managed by the hour and can result in better maintenance of parenteral nutrition.[4] There is a shorter time to recovery of renal function and better control of azotemia.[9, 10] CRRT has a potential anti-inflammatory capacity due to removal of cytokines and prevents the surge in intracranial pressure seen in ID.[11] Potential disadvantages of CRRT include increased cost, short filter life, and the need for anticoagulation.[4] Intermittent dialysis has disadvantages compared to CRRT. ID is limited in the amount of time that it can be performed daily. There is often associated hemodynamic instability. The resulting hypotension may lead to decreased renal recovery.

We hypothesize that renal function and hemodynamic stability in trauma and surgical ICU patients are better preserved by CRRT than ID.

Patients and Methods

Following institutional review board approval, a retrospective review of the medical records of patients admitted to the trauma or surgical services who required renal supportive therapy was performed. All patients were critically ill and in the intensive care unit. Indications for CRRT included 1) increasing potassium, 2) increasing BUN, 3) increasing creatinine, or 4) increasing extracellular fluid. Thirty patients received CRRT from June 1999 to February 2002. Twenty-seven patients received ID from December 1997 to December 1999. The study was controlled for severity of illness and demographics using Injury Severity Scores and APACHE II scores. Outcomes assessed included survival, renal function, acid-base balance, hemodynamic stability, and oxygenation/ventilation parameters. Statistical analyses were performed in SPSS version 10.0 and included *t* test and assessment for significance in change over time by slopes comparisons. Statistical significance is indicated by $P < 0.05$.

CRRT was performed in the ICU and was managed primarily by the surgical critical care staff. The usual mode of CRRT was continuous venovenous hemodiafiltration. ID was performed either in the ICU or in the dialysis unit and was managed by the medical nephrology staff. Vascular access was obtained by percutaneous placement of a double lumen catheter into either the subclavian, internal jugular, or femoral vein.

Results

Populations were similar across demographics and severity of illness as measured by APACHE II scores (Table 1). There was no statistical difference in duration of RRT, survival, or the need for dialysis after discharge (Table 2). Renal function, measured by creatinine clearance [(140 − age) × weight/([Cr] × 72)], was statistically greater with CRRT. There was better control of azotemia with CRRT: BUN was lower and creatinine was lower at the end of 7 days of treatment (Table 3). A statistically significant higher mean arterial blood pressure was maintained with CRRT ($P = 0.021$) by *t* test. Mean arterial blood pressure was 83.2 ± 11.3 in the CRRT group and was 76.2 ± 10.9 in the ID group. *t* test also demonstrated significance by a lower mean body temperature noted with CRRT ($P = 0.002$), and a higher partial thromboplastin time (PTT) ($P = 0.034$) with CRRT. Other parameters assessed did not reveal a difference between the two groups. Oxygenation and ventilation parameters included partial pressure of oxygen (pO2), fractional concentration of oxygen in inspired gas (FiO2), pO2:FiO2 ratio

TABLE 1. *Demographic Means*

	CRRT	ID	*P**
Age (years)	52.67 ± 18.2	55.15 ± 19.2	0.619
APACHE II	25.43 ± 5.3	26.04 ± 6.05	0.689
ISS	18.47 ± 19.4	10.07 ± 17.02	0.090
ICU LOS	44.10 ± 25.9	45.63 ± 39.5	0.862
GCS	7.20 ± 3.5	7.15 ± 3.3	0.954
Vent days	38.76 ± 25.2	40.41 ± 37.3	0.846
Pressor days	15.6 ± 13.8	15.27 ± 15.7	0.934

ISS, Injury Severity Score; ICU LOS, intensive care unit length of stay; GCS, Glasgow Coma Scale; Vent days, no. of ventilator use; Pressor days, no. days of vasopressor use.

* As measured by *t* test; $P < 0.05$ statistically significant.

TABLE 2. *Duration of RRT While in Hospital, Percentage of Patients Who Survived Until Discharge from the Hospital, and Percentage of Those Who Did Not Require Any Form of Renal Replacement Therapy at Discharge*

	CRRT	ID	P*
HD duration (days)	14.9 ± 7.8	19.7 ± 18.8	0.259
Survivors	46.70%	44.40%	0.866
Off HD	54.50%	37.00%	0.259

HD, hemodialysis.
* As measured by *t* test; $P < 0.05$ statistically significant.

TABLE 3. *Results of Means of Variables at Day 1, Initiation of Therapy, and at Day 7 of Therapy*

		CRRT	ID	P*
Creatinine	Day1	3.8 ± 1.9	4.8 ± 3.1	0.136
	Day7	2.1 ± 1.1	5.2 ± 2.8	0.000
BUN	Day1	89.2 ± 43.4	99.5 ± 46.1	0.387
	Day7	54.7 ± 18.2	100 ± 17.6	0.000
Cr clearance	Day1	39.4 ± 36.5	30.9 ± 22.4	0.311
	Day7	61.5 ± 38.4	33.1 ± 32.4	0.035

BUN, blood urea nitrogen.
* As measured by *t* test; $P < 0.05$ statistically significant.

(P:F), and partial pressure of carbon dioxide (pCO2). Acid-base balance measured by pH also was not significantly different between the groups (Table 4).

Discussion

A review of the literature comparing CRRT with ID overall suggests improved survival with CRRT. Many retrospective studies performed in the 1990s support improved survival.[12–20] There are two studies that show no advantage with CRRT.[21, 22] Two prospective randomized studies have been conducted. Kierdorf showed a survival advantage with CRRT,[23] whereas, Mehta showed decreased survival with CRRT but increased renal recovery in survivors.[24] Overall, there is insufficient evidence based on the current literature. Most studies are observational, have inadequate sample sizes, differences in patient characteristics (medical and surgical), and some patients received both treatment modalities. There are no trauma/surgical only studies. These studies suggest decreased mortality with CRRT when similar baseline severity of illness are matched and that sicker patients are more likely to get CRRT.[23, 25] Also, evidence suggests that CRRT may be the modality of choice for ARF with multiple organ dysfunction syndrome (MODS) and ID the choice for isolated ARF in stable patients.[25, 26]

Our study supports current literature showing hemodynamic stability and better renal function with CRRT *versus* ID. There was significant improvement in azotemia with CRRT as shown by lower BUN and Cr levels at the end of the study treatment period, as

TABLE 4. *Results of Means of Variables at Day 1, Initiation of Therapy, and at Day 7 of Therapy*

		CRRT	ID	P*
pO2	Day1	100 ± 24.3	99.9 ± 30.8	0.898
	Day7	102.5 ± 26.2	110.4 ± 50.7	0.550
P:F ratio	Day1	188.7 ± 77.8	193.4 ± 78.1	0.825
	Day7	213.2 ± 95.0	238.7 ± 89.8	0.477
pCO2	Day1	44.6 ± 10.4	43.9 ± 11.3	0.814
	Day7	45.6 ± 9.4	44.5 ± 7.4	0.748
pH	Day1	7.31 ± 0.07	7.34 ± 0.08	0.104
	Day7	7.37 ± 0.05	7.36 ± 0.05	0.385

pO2, partial pressure of oxygen; P:F ratio, pO2:FiO2 ratio; pCO2, partial pressure of carbon dioxide.
* As measured by *t* test; $P < 0.05$ statistically significant.

well as improvement in renal function measured by creatinine clearance. Although not statistically significant, there was a trend toward more patients treated with CRRT being off of HD at the time of discharge from the hospital (54% *vs* 37%). The duration of RRT was lower in the CRRT group but was not significantly different. There was no significant survival advantage seen with either modality. The cause of death in the majority of patients was multisystem organ failure; however, the exact cause of death was not evaluated in this study. The precise role of renal failure in contributing to death was not analyzed.

There was a statistically significant difference in the mean arterial blood pressure. Furthermore, the clinical significance of hemodynamic stability between these populations is best assessed through an evaluation of the standard deviation in the mean arterial blood pressure. In assessment of the standard deviation with intermittent dialysis, a subpopulation of patients undergoing therapy would have had mean arterial blood pressures in the mid-60s, indicating significant hemodynamic compromise. Patients undergoing CRRT, in the worse case scenarios considering the standard deviation of the mean, would have had blood pressures in the mid-70s. This difference is felt to be of clinical significance in an organ perfusion. The precise number of hypotensive episodes was unable to be determined in this retrospective review; however, there was no difference in vasopressor use between the two groups.

Although a statistically significant difference was found between mean body temperature and mean PTT in the two groups, there is no clinical significance between the values. The actual measured difference in temperature was only 0.5°C, with no patients sustaining refractory hypothermia. There were no adverse bleeding events noted during the study.

The study population consisted only of trauma and surgical critical care patients; no medical patients were included. The population was demographically similar between the CRRT and ID groups. There was no dif-

ference in age, APACHE II scores, injury severity scores, ICU length of stay (LOS), Glasgow Coma Scale (GCS), or ventilator days. Thus, our study represents a homogenous group of trauma/surgical ICU patients.

Limitations of this study are apparent. This was a retrospective chart review and there was not randomization to either group. Also, ID was performed between December 1997 and December 1999 and CRRT was performed between June 1999 and February 2002, two different time periods. The reason for this is related to the arrival of CRRT at our institution around May 1999. After the arrival of CRRT, it quickly became the modality of choice among the surgical critical care staff due to the relative ease of use and superior results. We also had a relatively small sample size consisting of a total of 57 patients. This study is unique in that we included only trauma and surgical ICU patients with ARF and that CRRT was performed by the surgical critical care staff while ID was performed by the medical nephrology staff.

In conclusion, continuous renal replacement therapy in this preliminary study results in an enhancement of renal function with improved creatinine clearance at the time of dialysis discontinuation. CRRT provides better control of azotemia while preserving hemodynamic stability in the critically ill surgical patient.

Acknowledgments

Thanks to Nathan W. Arp, B.S., Candice Scroggins, and Christopher E. Keel, B.S., for assistance with data management.

REFERENCES

1. Singri N, Ahya SN, Levin ML. Acute renal failure. JAMA 2003;289:747–51.

2. Kellum JA, Angus DC, Johnson JP, et al. Continuous versus intermittent renal replacement therapy: a meta-analysis. Int Care Med 2002;28:29–37.

3. 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 2002;40:875–85.

4. Abdeen O, Mehta RL. Dialysis modalities in the intensive care unit. Crit Care Clin 2002;18:223–47.

5. Mehta RL. Indications for dialysis in the ICU: renal replacement vs. renal support. Blood Purif 2001;19:227–32.

6. Kramer P, Wigger W, Rieger J, et al. Arteriovenous haemofiltration: a new and simple method for treatment of over-hydrated patients resistant to diuretics. Klin Wochenschr 1977;55:1121–2.

7. Van Bommel EFH, Bouvy ND, So KL, et al. Acute dialytic support for the critically ill: intermittent hemodialysis versus continuous arteriovenous hemodiafiltration. Am J Nephrol 1995;15: 192–200.

8. Vanholder R, Van Biesen W, Lameire N. What is the renal replacement method of first choice for intensive care patients? J Am Soc Nephrol 2001;12:S40–3.

9. Daxi JL, Dehua G, Honglang X, et al. A retrospective study of continuous renal replacement therapy versus intermittent hemodialysis in severe acute renal failure. Clin Med J 2001;114: 1157–61.

10. Bellomo R, Farmer M, Bhonagiri S, et al. Changing acute renal failure treatment from intermittent hemodialysis to continuous hemofiltration: impact on azotemic control. Int J Art Organs 1999;22:145–50.

11. Bellomo R, Ronco C. Continuous haemofiltration in the intensive care unit. Crit Care 2000;4:339–45.

12. Bellomo R, Ronco C. Continuous versus intermittent renal replacement therapy in the intensive care unit. Kidney Int 1998;53(Suppl):S125–8.

13. Golper T. Continuous arteriovenous hemofiltration in acute renal failure. Am J Kidney Dis 1985;6:373–86.

14. Maurtz W, Sporn P, Schindler I, et al. Acute renal failure in abdominal infection: comparison of hemodialysis and continuous arteriovenous hemofiltration. Anasth Intensivther Notfallmed 1986;21:212–7.

15. Silvester W. Outcome studies of continuous renal replacement therapy in the intensive care unit. Kidney Int 1998;53(Suppl): S138–41.

16. Van Bommel E, Ponssen HH. Intermittent versus continuous treatment for acute renal failure: where do we stand? Am J Kidney Dis 1997;30(Suppl):S72–9.

17. Bellomo R, Mansfield D, Rumble S, et al. Acute renal failure in critical illness: conventional dialysis versus acute continuous hemodiafiltration. ASAIO J 1992;38:M654–7.

18. Bellomo R, Boyce N. Continuous venovenous hemodiafiltration compared with conventional dialysis in critically ill patients with acute renal failure. ASAIO J 1993;39:M794–7.

19. Kruczynski K, Irvine-Bird K, Toffelmire E, Morton AR. A comparison of continuous arteriovenous hemofiltration and intermittent hemodialysis in acute renal failure in patients in the intensive care unit. ASAIO J 1993;39:M778–81.

20. Kierdorf H. Continuous versus intermittent treatment: clinical results in acute renal failure. Contrib Nephrol 1991;93:1–12.

21. Van Bommel E, Bouvy N, So K, et al. Acute dialytic support for the critically ill: intermittent versus continuous arteriovenous hemodiafiltration. Am J Nephrol 1995;15:192–200.

22. Jakob S, Frey F, Uehlinger D. Does continuous renal replacement therapy favourably influence the outcome of the patients? Nephrol Dial Transplant 1996;11:1250–5.

23. Kierdorf H, Sieberth H. Continuous renal replacement therapies versus intermittent hemodialysis in acute renal failure: what do we know? Am J Kidney Dis 1996;28(Suppl):S90–6.

24. Mehta R, McDonald B, Gabbai F, et al. A randomized continuous versus intermittent dialysis for acute renal failure. Kidney Int 2001;60:1154–63.

25. 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. Int Care Med 2002;28:1411–8.

26. Dunham CM. Clinical impact of continuous renal replacement therapy on multiple organ failure. World J Surg 2001;25: 669–76.