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Abstracts

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Patient Characteristics

1

Evaluation of the PRISMA M10 Circuit in Critically Ill Infants Requiring Continuous Renal Replacement Therapy (CRRT): A Report from the ppCRRT Registry Group

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Currently available extracorporeal circuits in the US often require blood priming to prevent hypotension/anemia in smaller pediatric patients. The PRISMA M10 circuit, composed on an AN-69 membrane with a blood volume of 50 ml is available in other countries, but has not been cleared by the FDA for use in the US. An IDE study of the M10 circuit was conducted in the US for use in critically ill pediatric patients with acute kidney injury <15 kg in size. The IDE study protocol allowed for maximal blood pump flow of 20 ml/min. Fifteen patients (9 M, 6 F, mean size 5.8 ± 2.8 kg, range 2.6–12.5 kg, age 4 d – 13 mo, mean creatinine = 1.2 ± 0.7 mg/dl) were studied at 4 Prospective Pediatric CRRT Registry Group centers. A total of 61 filters (range 1–4 circuits per pt) were used (mean circuit life 28.6 ± 22.5 hrs, range 1 to 74.5 hrs, 55% > 24 hrs) and no blood leaks occurred. All circuits achieved Qb 20 ml/min. 42/61 filters clotted and mean circuit life was lower for these filters than those changed for other reasons (23 ± 17 vs. 41 ± 28 hrs, *p* < 0.005). Mean total UF was 7893 ± 12962 ml (–148 to 40283 ml) with 12/15 patients surviving and 3/15 patients achieving dry weight. We conclude that the PRISMA M10 circuit can serve well for CRRT in small pediatric patients. Further research is needed to determine if higher blood pump flow rates would decrease clotting incidence and increase filter life span and ultrafiltration rates.

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Metabolic Acidosis in Patients with Liver Failure Undergoing Regional Citrate Anticoagulation for CVVHDF

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Background: Citrate anticoagulation is increasingly used for CRRT. Recently, it has been suggested that its use can be safe in patients with liver failure. However, significant complications, such as metabolic acidosis due to impaired citrate metabolism, can occur. **Methods:** We reviewed the utilization of citrate anticoagulation for CRRT in patients with hepatic injury in our center. For all patients, sodium citrate 4% was initiated at 220 ml/hr and adjusted to maintain postfilter ionized calcium between 0.25–0.35 mmol/L (1.0–1.4 mg/dl). Calcium chloride 1.5% was initiated at 20 ml/hr and adjusted to maintain systemic serum calcium between 1.0–1.3 mmol/L (4.0–5.3 mg/dl). Blood flow rate was 125 ml/hr. Sodium chloride 0.9% was infused at 1000 ml/hr as replacement fluid. The dialysate, composed of 4750 ml of Hemosol B0 solution (Gambro), was delivered at 1000 ml/hr after having discarded the 250 ml of NaHCO₃ solution. **Results:** Between January 2004 and September 2005, 15 patients underwent citrate anticoagulation for CVVHDF treatments, due to filters coagulation problems. Three patients presented with liver injury (acute ischemic liver injury, metastatic hepatocarcinoma with peripheral signs of cirrhosis, and chronic Child C cirrhosis). No modification was required to our citrate protocol and no complications occurred in 2/3 of cases. One patient (Child C cirrhosis) developed in <8 hours severe metabolic acidosis associated with increased total to ionized calcium ratio (>2.5), suggesting an accumulation of unmetabolized citrate. Bicarbonate levels decreased from 21 to 14 mEq/L. A bicarbonate perfusion and a reduction in the citrate perfusion rate did not correct the acidosis. The dialysate composition was modified to add the bicarbonate solution (250 ml) to the Hemosol B0 (4750 ml) solution and the dialysate infusion rate was increased to 2000 ml/hr. Bicarbonate levels returned to normal values and remained stable. **Conclusion:** Citrate anticoagulation may be used in patients with hepatic injury, but important precautions must be taken, especially in cirrhotic patients. Acid-base status and total to ionized calcium ratio should be closely monitored with concerns about metabolic acidosis and accumulation of unmetabolized citrate. In such cases, adjustments in the rate of bicarbonate, citrate and possibly calcium perfusions should be undertaken.

CRRT in Developing Countries

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This study is a retrospective analysis of aetiology and outcome of CRRT in patients with renal dysfunction and hemodynamic instability in a tertiary care centre in Kerala, India. All patients admitted to Medical College Hospital, Trivandrum requiring CRRT between the period January 1, 2003 to December 31, 2004 were included in the study. All patients in whom CRRT was discontinued within 6 hours due to any cause was excluded from the study. 66 patients were studied with a mean age of 41.74 ± 15.32 years. Male to female ratio was 1.75:1. Patients predominantly had acute renal failure (88%). 6% each had acute on chronic and chronic renal failure. 63.6% of patients survived. In spite of limitations due to financial constraints, (PD fluid was used as the dialysate, F8 dialyzer was used in many instances instead of CVVH filter, lack of adequate facilities for frequent biochemical monitoring), CVVHD remains an important modality of renal support in patients with renal dysfunction in developing countries.

RIFLE Classification Does Not Predict Outcome in Dialytic Acute Kidney Dysfunction

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Purpose: To prospectively determine the characteristics and prognosis of patients with Acute Kidney Dysfunction (AKD) who required dialysis support at the Intensive Care Unit (ICU) and to validate the RIFLE classification in this population. **Methods:** Over one year, 214 patients that were admitted to the ICU at three tertiary care hospitals and required renal replacement therapy (RRT) were studied. Patients with end-stage renal disease requiring chronic dialysis and those with ICU stay less than 24 h were excluded. AKD was classified according to RIFLE criteria. Data were collected at the start of RRT. Logistic regression was used in multivariable analysis and results are presented as odds-ratio and 95% confidence interval (OR, 95% CI). **Results:** The mean age was 71.4 years [standard deviation (SD) = 15.8]; 112 (52%) patients were males. The SAPS II and SOFA (except renal domain) scores were 47.9 (SD = 10.8) and 6.0 (SD = 3.1) points, respectively; 177 (83%) were on mechanical ventilation and 157 (73%) used vasopressors. The main reasons for AKD were sepsis (74%), ischemia/shock (72%) and drug/toxins (29%). Continuous RRT were initially used in 179 (84%) patients and the main indications for RRT were acidosis (72%), hypervolemia (50%), uremia (43%) and anuria (37%). According to RIFLE criteria, patients were classified as risk (n = 54, 25%), injury (n = 58, 27%) and failure (n = 102, 48%). The overall mortality rate was 76% and there were no differences according

to the RIFLE classification (risk = 72%, injury = 79% and failure = 76%, p = 0.681). The final model of multivariable analysis was: age (years) [OR = 1.04 (1.01–1.31), p = 0.004], need of vasopressors [OR = 2.72 (0.99–7.49), p = 0.053; presence of comorbidity (Charlson index >1) [OR = 2.75 (1.01–7.51), p = 0.048], impaired functional capacity [OR = 7.69 (2.33–25.42), p = 0.001] and more than two associated organ failures [OR = 10.66 (2.13–53.35), p < 0.001]. The RIFLE classification was forced into the model and was not selected. **Conclusions:** Age, need of vasopressors, more than two associated organ failures, the presence of comorbidity and a previous reduced functional capacity were significantly related to a higher mortality in this population. The RIFLE classification did not discriminate the prognosis in the ARF patients who underwent dialysis support in the ICU.

Therapy induced Alkalosis Is Not Associated with Increased Mortality in Intensive Care Unit (ICU) Patients on Continuous Renal Replacement Therapy (CRRT)

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Background: Acid-base disorders are common in critically ill patients. Once CRRT is initiated, it becomes a major determinant of acid-base status. We hypothesized that therapy induced alkalosis is associated with increased hospital mortality. **Methods:** Prospective observational cohort of ICU patients requiring CRRT at the Cleveland Clinic between 1995 and 2001. 274 patients who were on bicarbonate based CRRT for 3 days or more, and had arterial pH measurements on day four were included in the study. Acid-base status was analyzed after 3, 5, and 10 days of CRRT (acidosis pH < 7.35, alkalosis pH > 7.45). Univariate, followed by multivariate linear regression analyses were performed when appropriate. Mixed modeling (proc mixed) was used in analyzing repeated measures. All statistical analyses were performed with SAS v8. **Results:** Baseline characteristics: Age 59.7 ± 15 yrs, 64% male, dose of dialysis 15.6 ± 6.5 mL/kg/hr, pH 7.38 ± 0.1 , CO_2 21.2 ± 4.5 mmol/L, PaCO_2 37.6 ± 10.8 mmHg. In univariate analysis, at day 3, 5, and 10, alkalosis was not associated with increased mortality compared to normal pH (39.2 vs. 41.7%, 37.0 vs. 36.5%, 34.3 vs. 39.3%). But acidosis was associated with higher mortality at day 3 and 5 (65.4 vs. 41.7%, p = 0.004, 60 vs. 36.5%, p = 0.04). Independent predictors of pH are shown in table 1. Non-survivors had lower pH initially and throughout CRRT after adjusting to potential confounders using mixed modeling, see figure 1. **Conclusion:** Alkalosis during CRRT is not associated with increased mortality. Acidosis at initiation and during CRRT was associated with increased mortality.

Table 1. Independent predictors of pH at days 3, 5 and 10 by multiple linear regression

Variables*	Day 3		Day 5		Day 10	
	Parameter estimate	P value	Parameter estimate	P value	Parameter estimate	P value
CO ₂	0.013	<0.0001	0.015	<0.0001	0.012	<0.0001
Anion gap			0.004	<0.0001		
PaCO ₂	-0.008	<0.0001	-0.008	<0.0001	-0.008	<0.0001
Respiratory failure			0.023	0.008		
Dialysis dose	0.00004	0.03	0.00005	0.01		
WBC count			-0.001	0.004		
Adjusted R ₂	0.75		0.76		0.70	

* Variables included in the preliminary multiple linear regression model were: age, gender, PaCO₂, mean arterial pressure, dialysis dose, WBC count, anion gap, BUN, and mechanical ventilation.

Figure 1. Non-survivors had lower pH values at initiation that persisted throughout CRRT.

*Adjusted for age, gender, dialysis dose, CO₂, PaCO₂, BUN, hematocrit, aniongap, log urine output, mean arterial pressure, pressor requirements, and mechanical ventilation.

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CRRT in Pediatric Sepsis: A Report from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group

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CRRT has become more prevalent in the management of fluid overload (FO) and electrolyte imbalance in pediatric patients with Acute Kidney Injury (AKI). Since 01/01/01 115 of 370 patients enrolled in the 13-center ppCRRT Registry have a primary or secondary diagnosis of sepsis. Complete data for 102 patients with sepsis were available for analysis. Median age was 7.32 years (range 2 days – 25.11 years), 44 (43%) were female, 61 (60%) received diuretic therapy, 81 (79%) had MODS and 83 (81%) required ventilatory support. CRRT modalities were CVVHD (52%), CVVH (26%) and CVVHDF (22%). Indications to initiate CRRT were fluid and electrolyte abnormalities (54%), FO only (38%) and electrolyte abnormality only (8%). 57 (56%) patients survived (S) and ventilated patients had similar S as non-ventilated patients (53% vs. 68%, $p = 0.22$). There was no significant difference in the S rate among CRRT modalities [CVVHD (47%) vs. CVVH (67%) vs. CVVHDF (64%), $p = 0.19$]. Survivors had lower FO at CRRT initiation and Paw at CRRT termination.

	Survivors (S)	Non-survivors (NS)	P value
Age (yrs)	9.01 ± 0.93	8.07 ± 1.04	0.50
Initial PRISM 2	14.08 ± 1.25	17.00 ± 1.36	0.07
Initial Paw	19.27 ± 1.59	20.89 ± 1.69	0.40
FO at CRRT (%)	15.45 ± 3.85	28.13 ± 4.33	<0.05
GFR	30.43 ± 3.25	29.82 ± 3.17	0.96
CVP (cm H ₂ O)	16.37 ± 1.26	17.87 ± 1.32	0.41
Number of pressors	1.58 ± 0.15	1.88 ± 0.17	0.19
Time ICU to CRRT (days)	4.73 ± 2.46	10.60 ± 2.70	0.11
CRRT duration (days)	9.50 ± 5.30	19.25 ± 6.03	0.26
UF volume (ml)	50570.87 ± 6931.30	44749.8 ± 7800.92	0.57
Clearance (ml/hr/1.73 m ²)	2217.01 ± 60.50	2650.56 ± 174.90	<0.05
Paw at end CRRT	10.84 ± 1.27	19.72 ± 1.30	<0.05

All values are mean ± SE.

These ppCRRT Registry data show: (1) significant difference between S and NS in FO% at initiation of CRRT, (2) improvement in S pulmonary status at the end of CRRT and (3) a trend toward improved survival with convective therapy. We suggest (1) early CRRT initiation after resuscitation to balance fluid status may improve both pulmonary function and survival in pediatric patients with sepsis and (2) the currently accepted belief that convective therapy offers therapeutic advantage over diffusion may be justified.

Incidence, Clinical Predictors and Outcome of Acute Renal Failure Among Trauma Patients: A Prospective Multicenter Study

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Data on epidemiology, clinical predictors and outcomes of acute renal failure (ARF) among severe trauma patients is limited and mostly retrospective in nature. The incidence of ARF varies between 0.1–8.4% due to inconsistent definitions of ARF. Several retrospective studies reported high mortality of 40–70% for trauma patients with severe ARF. We performed a secondary analysis of an existing database of the 'Inflammation and the Host Response to Injury' (Glue Grant) study which prospectively collected clinical data on patients with severe trauma in multiple clinical centers. ARF was defined using recently published Rife criteria on the basis of the change in the serial serum creatinine values. 727 patients' data were assessed from database. Complete data were available for 561 patients. After review of each individual patient file, we identified 109 (19%) patients with ARF as defined by Rife criteria: 35% with Rife-Risk (R), 32% with Rife-Injury (I) and 33% with Rife-Failure (F). Patients who developed ARF were more likely to be older Caucasian males. Significantly lower systolic but not diastolic or mean arterial blood pressures in emergency room (ER), but not on the scene of accident, characterized patients who developed ARF. Serum lactate levels in ER were also significantly higher among patients who later developed ARF. APACHE II score at the time of ICU admission was significantly higher among ARF patients. These patients had prolonged ICU hospital stay, required longer mechanical ventilation and more use of steroids. Hospital mortality (42%) was significantly worse for patient with ARF, compared to patients with normal renal function (17%). Patients with ARF had significantly higher prevalence of both infectious and non-infectious complications. Sepsis and multi-organ failure were more common causes of death among patients with ARF.

Figure 1.

Hospital mortality was correlated to the severity of ARF and was 29%, 43% and 56% for patients with Rife-R, Rife-I and Rife-F, respectively (fig. 1). Incidence of ARF among trauma patients may be higher than previously reported. ARF is a severe complication with significantly increased hospital morbidity and mortality, and severity of ARF correlates with adverse outcomes.

Temporary Vascular Access for Renal Replacement Therapy (RRT) – Predictors of Resource Utilization in an Inner City Population

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Temporary Vascular Access (TVA) plays a significant part in delivery of RRT both in patients already on dialysis (with either a transient complication in the usual access or due to absence of an AV access), and also in patients with Acute Renal Failure (ARF). Placement of TVA's, follow-up, associated complications and the high risk of the patients in question requires a significant proportion of the available healthcare resources. **Methods:** A randomized retrospective chart review (n = 120) was used to analyze the length of stay and factors predicting the utilization of resources in an inner city population, admitted to our facility requiring a TVA during years 2003 and 2004. **Results:** Mean age of the sample was 65.6 ± 15.8 years (Males – 60; Females – 60). A majority of TVA (69.7%) were required for complications in the existing access, 23% for people with acute deterioration in chronic renal disease and 7.3% in patients with ARF (no preexisting renal disease). The most common complications in the usual access were thrombus formation (68.2%), sepsis (24.7%) and bleeding (4.7%). Average hospitalization was 11 days after adjusting for outliers. A weekend admission, absence of a primary care physician, ARF, sepsis or bleeding complicating the usual access, significant co-morbidities (≥4), Serum Albumin, Age, Gender, Race, Training or background of the physician performing the procedure, Insurance status, Type of insurance did not show any association with the same. **Conclusion:** Our research highlights the presence of significant predictors for utilization of resources in an inner city population requiring a TVA for RRT. Further research to understand the impact of the same in larger populations and on developing innovative methods to reduce patient morbidity and better manage the ever shrinking health care resources is required.

Short-time Results Treatment on CRRT in Department of Nephrology in Podgorica

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The patients with ARF (acute renal failure) have been treated by use of one of the CRRT methods for the first time in the Clinical Center Podgorica since 2004. We have provided the apparatus multifiltrate made by Fresenius company for hemodialysis of our ARF patients. Our aim with this study is to show and share the results we have achieved in order to improve our further work as well as to acquire new knowledge and to be criticized in goodwill. The data given in this study relate to the period from 01.07.2004–01.11.2005. All our patients were treated with CVVHDF, original kit 8, Fresenius M.care. The number of the patients treated during this period was 13 (11 male patients and 2 female). Average age of male patients was 51.7 and of female patients was 51.5. 12 patients out of 13 treated, developed ARF for the first time while with one female patient renal failure had already been verified and in the noted period got worse. ARF etiology of our patients was as follows:

- 4 patients suffered from Cholecystopancreatitis.
- 4 patients had undergone cardio vascular surgery.
- 2 patients had undergone triple ACBP.
- 2 patients had aneurysmectomy on abdominal.
- 1 patient had just had cesarean section (8 pregnancy, 3 living babies). ARF was caused by severe hypervolemia and hemorrhagic syndrome. In the further treatment primary antiphospholipid syndrome was diagnosed.
- 1 patient suffered from hemorrhagic pulmonary renal syndrome with previously verified hemorrhagic fever – Hantavirus positive.
- With 1 patient a GN-membranosa glomerulosa was diagnosed by use of biopsy and the patient developed pulmonary hemorrhagic syndrome as well.
- The last two patients had sepsis which caused the development of ARF. The colostoma infection was preceded by adenocarcinoma colon surgery and incomplete artificial abortion.
- The level of nitrogen substances was: urea 14–39.6 mmol/L; creatinine 280–86 mmol/L.
- The average duration of CVVHDF was 20.65 hours. The longest treatment was on the patient suffered from antiphospholipid syndrome and it lasted 49 hours.
- The average dose of anticoagulation with heparin was 800–1300 IU/h.

Arterial pump of 200–250 ml/h the flow of substances for dialysis was 700–1200 ml/h substituents 1000–1500 ml/h. The value of UF with 12 patients was 450–600 ml/h and with 1 patient UF was 800–100 ml/h. Total recovery with patients who suffered from primary antiphospholipid syndrome, while total recovery of renal function was achieved with 6 patients, 2 patients died and the evaluation of the treatment was not possible. The female patient with renal failure previously verified did not show any sign of renal function recovery. The treatment was continued with chronic hemodialysis. The remained 4 patients treated with this method did not show overall improvement neither the ARF was resolved. **Conclusion:** This was a modest experience; the choice of indications was not quite good, there was no coagulation incidents, necessary replacements of membranes every 8–10 h.

Demographic Characteristics of Pediatric CRRT: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group

J.M. Symons, M.J.G. Somers, M.A. Baum, T.E. Bunchman, P.D. Brophy, D. Blowey, J.D. Fortenberry, D. Chand, F.X. Flores, R. Hackbarth, S.R. Alexander, J. Mahan, K.D. McBryde, S.L. Goldstein

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Since 1/1/01, 346 patients from 13 US centers have been enrolled in the ppCRRT registry. We now report demographic characteristics and outcomes for 342 patients with complete data. Ages were newborn to 25 years, 59% males, weights 1.3–160 kg (mean 33.7 kg, median 24.2 kg). Subjects averaged 5.7 days in ICU prior to CRRT (range 0–135, median 2). At CRRT initiation, 48% were on diuretics and 66% were on vasoactive drugs. The table lists indications for CRRT and principal diagnoses. 27% received CVVH alone; 48% received CVVHD alone; others received multiple modalities. Mean blood flow (Q_B) was 97.9 ml/min (range 10–350 ml/min, median 100 ml/min); mean Q_B per body weight was 5 ml/min/kg (range 0.6–53.6 ml/min/kg, median 4.1 ml/min/kg). Days on CRRT were <1–83 (mean 9.1; median 6). Overall survival was 58%. Survival was lowest when CRRT was started for combined fluid overload and electrolyte imbalance. There was better survival in subjects with principal diagnoses of drug intoxication, renal disease, tumor lysis syndrome, and ischemia/shock; survival was lowest in liver disease and bone marrow transplant. Survivors and non-survivors were not significantly different for other reported demographic data. We conclude that CRRT can be used successfully for a wide range of critically ill pediatric patients and that patient survival is best for those with acute, specific abnormalities who lack multiple organ involvement. Earlier use of CRRT may lead to better outcomes; sicker patients with selected diagnoses may have lower survival.

	N	Survivors	% Survival
Indications for CRRT:			
Fluid overload and electrolyte imbalance	153	79	52
Fluid overload only	100	61	61
Electrolyte imbalance only	44	30	68
Prevent fluid overload to allow intake	11	7	64
Other	34	23	68
Principal Diagnoses:			
Sepsis	92	51	55
Bone marrow transplant	55	25	45
Cardiac disease/transplant	37	20	54
Liver disease/transplant	30	9	30
Malignancy (no tumor lysis syndrome)	29	15	52
Renal disease	27	25	93
Inborn error of metabolism	18	12	67
Ischemia/shock	16	13	81
Drug intoxication	12	12	100
Tumor lysis syndrome	11	9	82
Pulmonary disease/failure	8	5	63
Other	7	4	57

Comparison of Continuous Veno-Venous Hemodialysis with Intermittent Peritoneal Dialysis in ICU Setting

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Intermittent Peritoneal Dialysis (IPD) using a stylocath is an easy, cost effective & less cumbersome means of renal replacement therapy which can be easily done in Intensive Care Unit (ICU). This study was designed to compare IPD with Continuous Veno-venous Hemodialysis (CVVHD) in ICU settings. A total of 130 patients (65 in CVVHD group, 49 males & 16 females mean age 50.12 ± 17.45 yrs & 65 patients in IPD group 47 males 18 females mean age 48.24 ± 16.24 yrs) were retrospectively studied.

In CVVHD group 21 (32.3%) & in IPD group 23 (35.4%) patients survived (statistically NS). In both groups survival correlated with lower APACHE score & higher MAP at 0, 8, and 24 hrs (P value <0.001 in both groups). The URR (urea reduction ratio) was higher in survivors in both groups as compared to non survivors. S/Albumin at baseline was significantly higher in survivors than non survivors in both groups (2.73 ± 0.81 gm/dl vs 2.34 ± 0.52 in CVVHD gr & 2.80 ± 0.90 gm/dl vs 2.41 ± 0.62 in IPD group) Patients in IPD group were sicker with low mean arterial pressure (MAP) requiring inotropic support, (73.8% in IPD vs 58.4% in CVVHD group).

In conclusion IPD offers comparable Survival advantages in critically sick patients with renal failure in ICU settings with low cost.

Emerging Concepts in ARF and CRRT

Implementing a New Technology in a Clinical Setting: The Ingredients for Success

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Due to ongoing technological development, it is common for critical care units to face change. No matter how many benefits are to be derived from a change, implementing it remains a challenge. The Lewin's model provides a structured approach which facilitates the implementation of a change. This model has been use in our hospital to introduce the Prismaflex. The first phase of Lewin's model consists of analyzing the situation and brainstorming on the plan of actions. During this first phase, we identified and analyzed the many changes related to nursing practice affected by the transition from the Prisma to the Prismaflex. The information was obtained by meeting with Gambro's specialists and attending a six-hour training session for super users. Afterwards, the Clinical Nurse Specialist in collaboration with the

medical and nursing teams revised the current hemofiltration orders and protocols to make them appropriate for the new technology. We completed the first phase of the Prismaflex implementation with a three-hour training session provided to the Prisma certified Nurses. Then comes the implementation phase, in which the technology is introduced in the clinical setting. During this phase, support to the users is crucial. In order to provide this support, two Gambro specialists remained on-site until the users felt comfortable with the Prismaflex and 24/7 phone support was available. Unit resource people would regularly be present at the bedside to help users troubleshoot any arising issues. The last phase of the Lewin's change process consists of restoring the practice into a steady state. Hence, the most frequently encountered issues and their solutions were regularly communicated to the nursing team. Meetings were also held with Gambro specialists on an on-going basis to resolve outstanding issues and to discuss new findings on the hemofiltration therapies. Our experience revealed that to be a success, the implementation of a new technology must be well planned and resource personnel's time opened up to support users effectively.

Extracorporeal Blood Purification (ECBP) in Adult Respiratory Distress Syndrome (ARDS)

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Aim: To determine the beneficial effect of ECBP over respiratory and hemodynamic parameters in ARDS. **Material and Methods:** 16 patients of ARDS were subjected to CVVH/CVVHDF. Multi organ failure (MOF), ARDS were defined as per the American-European consensus conference and ACCP/SCCM consensus conference committee guide lines and ARF as base line normal creatinine increasing to >2.5 mg with in 24 hours. Routine labs and imaging studies including echo were performed. Replacement exchange volume, dialysate flow and blood flow rates respectively were 10–20 ml/kg/h, 1 liter/hour and 100 ml/mt. **Results:** There were 12 males. Average age was 50.5 years. The diseases associated – post operative 6, pneumonia 2, pancreatitis 3, necrotizing fasciitis 2, burns 2, poly trauma with poly transfusion 1. Underlying sepsis was considered in 14 and ARF in 4. Ventilatory and inotropic support was initiated in 14. CVVH ($n = 12$)/CVVHDF ($n = 4$) started with in six hours in 6 and after six hours in remaining after admission into ICU. Average duration of procedure was 42 hours (range 20–64 hours). Inotropic drug dose or number of drugs was reduced after >24 hours in 7 (50%), with significant improvement in mean arterial pressure mean arterial blood pressure from 55 ± 3 mmHg to 70 ± 4 mmHg. Respiratory parameters – O_2 saturation ($89\% \pm 1.2 \rightarrow 95.2\% \pm 4.2$) PEEP level ($8.2 \pm 3.5 \rightarrow 6 \pm 4.2$ cmH₂O) respiratory rate ($28.4 \pm 4.8 \rightarrow 18.2 \pm 5.1$), SpO_2/FiO_2 ratio ($117.33 \pm 4.2 \rightarrow 2.11 \pm 2.6$) improved in 12 (75%). Normalization of chest X ray was noted in all responders, and in 4 (25%) non-responders. Five patients – 4 patients in whom procedure initiated with in 6 hours in 1 patient after 6 hours including 2 patients who did not require ventilator or isotropic support recovered, rest succumbed to MOF. Patient survival rate was 31.25% ($n = 5$) and renal recovery rate was 43.75%

(n = 7). No significant complications observed related to procedure.
Conclusions: ECBP is safe, simple, adjuvant support therapy in ARDS with a beneficial role over pulmonary and hemodynamic functions, but needs to be initiated early and before requiring the ventilatory or high dose inotropic support for the best outcome.

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Continuous Renal Replacement Therapy in a Burn ICU: Launch of a Program

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Background: Access to Continuous Renal Replacement Therapy (CRRT) at our institution was previously non-existent. Application of high-volume continuous venovenous hemofiltration (HVCVVH) in

patients with multiple organ failure is controversial and not universally considered a proven treatment modality. Severely burned patients have a high mortality with many developing acute renal failure as one component of their multiple system failure. Early initiation of therapies such as CRRT and application of HVCVVH in select patients may be beneficial. **Objective:** To describe the steps taken to successfully implement an independent CRRT program in a burn ICU. **Main:** A medical intensivist with credentials to prescribe CRRT was hired by the institution. In addition, a medical consulting firm assisted in product selection and acquisition, development of order sets, flow-sheets, nursing and physician standard operating procedures, and assistance with meeting competency standards for all the staff. Two months prior to launch, weekly multi-disciplinary meetings were held to discuss various developmental issues. A month prior to the launch, the consulting firm delivered eight 90 minute introductory didactic sessions reaching approximately 90% of the ICU staff working various shifts. A week prior to launch, our CRRT machine vendors delivered a week long intensive training camp for 10 'super-users', consisting of both RNs and LVNs, previously identified by the institution. Satisfactory completion of a comprehensive competency checklist along with a grade of 85% or higher on a proficiency exam were required to be recognized by our institution as a 'super-user'. These 'super-users' were then tasked to train the rest of the nursing staff. Our first patient was successfully treated using our new machine a week later. A case series with lessons learned will be presented. **Conclusion:** Implementation of a new CRRT program in a previously naive ICU can be a daunting task. With focused application of various resources, along with institutional support, we have successfully initiated this new capability in a Burn ICU.

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Hemodiafiltration in Intensive Care Unit: Single Centre Experience from India

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Introduction and Purpose of the Abstract: The incidence of acute renal failure (ARF) in the hospital setting is increasing. It portend excessive morbidity/mortality and a considerable burden on hospital resources. In developing country like India it presents an excessive burden over limited resources. Extracorporeal therapies are the latest technology to show promise in the management of critically ill ARF. It is said that the potential of such a therapy goes beyond providing solely renal support. Global blood purification and removal of multiple inflammatory mediators. This system is being labelled as MOST (Multiple Organ Support Therapy). However, the available results are contradictory. **Aim:** To analyse the clinical setting and outcome of critically ill ARF patients managed with continuous renal replacement therapy (CRRT) and to assess utility of SOFA (Sequential Organ Failure Assessment) score in predicting outcome of CRRT. **Methodology:** From January 2004 to November 2005, 50 hemodynamically unstable cases of ill ARF underwent CVVHDF in intensive care unit. Hemodynamic instability was defined as systolic BP < 100mmHg in spite of one or more inotropic agents. SOFA score before initiation of dialysis support was recorded in all cases. SOFA score determines organ

failure in six systems. Score of 0–4 is awarded for each system. The total score may vary from 0–24. Higher the score, severe is the disease. Complete renal profile including ultrasound was done in all cases. CVVHDF was performed using Diapact Braun CRRT machine. Vascular access used were – Femoral in 32, Internal Jugular in 8, AVF in 4 and Subclavian 6 patients. 1.7% P.D. fluid was used as dialysate. 0.9% NS with addition of 10% Ca gluconate, Magnesium sulphate, Sodabarbonate and Potassium chloride added sequentially in separate units were used for replacement, carefully monitoring their levels. Anticoagulation of extracorporeal circuit was achieved with systemic heparin in 21 and regional heparin in 5 patients. No anticoagulation was used in 24 patients. **Results:** Of the 50 patients studied, 29 were males and 21 females (1.4:1). The average age was 52.88 yrs (20–75). The co-morbidities included – Type II DM in 29 (58%), Hypertension – 20 (40%), Coronary artery disease – 13 (26%) and Chronic kidney disease in 8 (18%) patients. Cause of ARF included Sepsis in 24 (48%), Hemodynamically mediated in 18 (36%) and acute over Chronic renal failure in 8 (16%) patients. The mean pre-dialysis systolic and diastolic BP was 92.28 and 61.19 mmHg respectively. 31 (62%) patients were ventilated. The mean duration of CRRT was 27.51 hours. The mean ultrafiltration rate was 71.80 ml/hr. Pre-dialysis serum creatinine, blood urea, serum bicarbonate and serum potassium levels were 6.05 mg/dl, 126.81 mg/dl, 14.94 mEq/l and 4.94 mEq/dl respectively. The overall mortality was 74%. Average SOFA score was 14.22. The variables influencing survival vs. mortality were – serum creatinine (4.31 vs. 6.93, $p = 0.02$), blood urea (111.33 vs. 134.56, $p = 0.02$), serum bicarbonate (18.34 vs. 11.96, $p = 0.05$) and SOFA score (11.42 vs. 15.33, $p = 0.02$), while blood pressure, serum potassium, mechanical ventilation and UF rate did not affect outcome. Common complications observed during the therapy included Hypokalemia in 19 (38%), Hyperglycemia in 17 (34%) and Hypophosphatemia in 16 (32%) patients. **Conclusions:** (1) Despite impressive advances in treating critically ill patients, mortality is dismally high. (2) Multiorgan dysfunction (as assessed by SOFA score) adversely affects outcome of CRRT. (3) SOFA score is useful predictor of outcome. (4) Level of azotemia and severity of metabolic acidosis are important predictors of outcome. (5) Monitoring of electrolytes, specially Potassium, Phosphorous and Sugar is mandatory.

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Citrate Accumulation Depends on the Dose of Hemofiltration in Patients on CVVHDF with Liver Dysfunction

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Background: We had previously reported that regional citrate anticoagulation during continuous veno-venous hemodiafiltration (CVVHDF) does not lead to citrate accumulation in patients with liver dysfunction. The current study evaluated the effect of filtration on citrate accumulation in acute renal failure patients with liver dysfunction who received CVVHDF using citrate as anticoagulant. **Methods:** We retrospectively reviewed 17 patients who underwent CVVHDF between May 2004 and October 2005. Group A (N = 7; 6 males and 1 female with a mean age of 51 years) received replacement fluid BGK2/0 at 1000 ml/hr between September 2004 and April

2005. Group B (N = 10; 6 males and 4 female with a mean age of 65 years) received replacement fluid BGK2/0 at 1500 ml/hr between May 2005 and October 2005. Citrate Dextrose-Formula A (ACD-A) was initiated at 150 ml/hr. The rate was adjusted to maintain post filter iCa between 1.0–1.4 mg/dl. Calcium chloride was administered as continuous intravenous infusion to maintain systemic serum iCa between 4.0 to 4.5 mg/dl. Blood flow rate was 100 ml/min. Prismaate BGK 0/3.5 (Gambro, USA) in 4 patients and Prismaate BGK 4/2.5 in 13 patients was delivered at 500 ml/hr as a dialysate. Serum and effluent citrate levels were measured daily. Systemic and post filter serum ionized calcium were measured one hour after initiating CVVHDF and then every six hours. **Results:** Data is summarized in the table. **Conclusion:** Serum citrate levels are significantly lower in the group receiving higher dose of filtration. Hemofiltration appears to be the major route of citrate elimination in these patients.

Variables	Group A (N = 7) Mean $\pm$ SD	Group B (N = 10) Mean $\pm$ SD	P value
AST (IU/l)	2130 $\pm$ 3130	2280 $\pm$ 3480	NS
Total bilirubin (mg/dl)	7.0 $\pm$ 5.05	7.73 $\pm$ 6.1	NS
ACD-A (ml/hr)	117.2 $\pm$ 47.4	143.2 $\pm$ 62.8	NS
Pre filter iCa (mg/dl)	3.4 $\pm$ 0.32	4.2 $\pm$ 0.61	<0.001
Post filter iCa (mg/dl)	1.7 $\pm$ 0.45	1.6 $\pm$ 0.14	NS
Serum citrate (mg/dl)	4.8 $\pm$ 2.3	2.0 $\pm$ 1.0	<0.001
Effluent citrate (mg/dl)	59.2 $\pm$ 23.41	70.4 $\pm$ 13.01	NS

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Apheresis in Critical Renal Diseases

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Objective: To observe the effects of plasma exchange (PE) and Immunoabsorption (IA) on the critical renal diseases. **Method:** 67 patients with critical renal diseases were enrolled and treated with PE and IA from 2000 to 2004, including males 31 and females 36, aged from 9 to 84 years (45.84 ± 17.13). The etiology of diseases included multiply myeloma (MM, n = 13), lupus nephropathy (LN, n = 12), thrombotic thrombocytopenic purpura (TTP, n = 3), hemolytic uremia syndrome (HUS, n = 5), ANCA associated vasculitis (MPA or WG, n = 8), macroglobulinemia (n = 3), fulminant hepatitis (n = 2), anti-GBM syndrome (n = 1), erythroderma (n = 1) and others (n = 9). **Results:** These patients were treated with single membrane plasma exchange (SPP) 51 patient-times, double filter plasma exchange (DFPP) 123, IA 18, SPP plus DFPP 5 and DFPP plus IA 3. Each patient received these therapies for 3.04 times, 2.9 liter of plasma in average. After the treatment, in the 3 TTP patients the platelet increased from $42.88 \pm 40.48 \times 10^9/L$ to $199.86 \pm 41.77 \times 10^9/L$ and hemoglobin from $57.63 \pm 32.25 g/L$ to $111.43 \pm 13.25 g/L$; in the HUS patients, the impaired renal function recovered in 5 cases, one patient entered the maintenance dialysis and 3 patients died; the IgM level in all the patients with macroglobulinemia reduced significantly; in all LN (type IV), the titers of anti-ds-DNA antibody and immunoglobulin (IgG) decreased from $27.35 \pm 21.45 mg/dl$ to $8.79 \pm 13.97 mg/dl$ and from $738 \pm 361 mg/dl$ to $438 \pm 262 mg/dl$, respectively, and positive ANA in 2 patients turned to negative; in the

13 MM patients (11 with type IgG and 2 with type IgA), the levels of IgG and IgA decreases from 4898 ± 4724 mg/dl to 2645 ± 2698 mg/dl and from 4829 ± 6625 mg/dl to 1165 ± 2430 mg/dl, respectively and hemoglobin increased from 56.0 ± 3.0 g/L to 83.8 ± 27.9 g/L, and the level of serum creatinine decreased in 4 patients, no change in 5 patients and increased in one patient; in all the vasculitis patients, the titers of ANCA reduced, and the renal function recovered in one patient, improved in 4 patients and maintenance dialysis in 3 patients.

Conclusion: Plasma exchange can treat TTP effectively. PE down-regulated the abnormally increase of immunoglobulin, light-chain protein presented in myeloma, furthermore, combined with chemotherapy could attenuate the renal function loss, promoted the survival rate. PE could cleanse the auto-antibody markedly, and decrease the titer of anti-ds-DNA antibody more efficiently. PE is recommended to treat the severe case of LN, LN + APS, TTP/HUS. To the macroglobulinemia patients, we recommend PE or IA combined with chemotherapy in short period. PE and IA have significant effects on the treatment of TTP/HUS, MM, macroglobulinemia, critical lupus nephropathy, but the future effects need to be further investigated.

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Evaluation of Different Blood Purification Modes in Acute Renal Failure (ARF)

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Objective: To applicate different techniques of blood purification in ARF, and thus to improve the outcome and level of medicare.

Methods: Among 191 ARF patients undergoing blood purification, we assessed corresponding prognosis in different modes such as intermittent HD (iHD), continuous veno-venous hemofiltration (CVVH), slow low extended dialysis (SLEDD), continuous ambulatory peritoneal dialysis (CAPD), and CVVH combined with iHD in different types of ARF. **Results:** One hundred and ninety-one ARF patients were undergoing blood purification, which was accounting for 34.6% of total ARF during the same period. Among them, 120 males and 71 females with mean age of 49.14 ± 19.61 yrs, serum urea level of 24.35 ± 14.31 mmol/L, serum creatine levels of 533.98 ± 397.21 μ mol/L. The average clearance of creatine was 17.61 ± 5.43 L/24 h according to the C-G formula. Dialysis modality included 101 on iHD, 57 on CVVH and SLEDD associated with PE (14) and IA (3), 16 on CAPD. The indications for CVVH or SLEDD included complicated ARF such as acute rhabdomyolysis syndrome, severe systemic vasculitis, congestive heart failure with unstable circulating blood volume, hypotensive shock, encephalic edema, ARDS, hypercalcemia crisis, SIRS, acute pancreatitis complicated ARF, malignancy, ARF after cardiac operation, hepatic encephalopathy and liver transplantation with multiple organ dysfunction syndrome (MODS). Pre-dilution CVVH was conducted with 150–200 ml/min blood volume, once per day or every other day until the recovery phase or transferring to maintenance HD, the replacement fluids were 4–6 liters per hour, the treatment time were 8–12 hours, with Fresenius F60 filter. The combination of CVVH and iHD were given in liver transplantation and hepatic encephalopathy especially with hyperbilirubinemia. The survival rate of CVVH was 35/57 (61.4%), the mortality was 38.6%

with 5 hemorrhage and 4 hypotension. iHD were performed only in those ARF without complications, the frequency was every other day, the treatment time was 5 hours, the survival rate was 70/101 (69.3%), 25 were died and 6 were losing follow-up (30.7%). CAPD were performed in Child and elderly patients. Among 16 CAPD patients, the recovery rate was 31.3%, the mortality 43.8%, and 24.9% lost follow-up. The total outcome of 191 ARF showed 47.1% with recovery 18.8% transferring to maintenance hemodialysis, 30.9% death and 3.2% lost follow-up. **Conclusions:** (1) In ARF, dialysis should be started early. Intensive and early dialysis plays a key role in the prognosis of ARF. (2) Considering with the efficacy of CRRT and iHD, data from ARF prognosis showed no significance. It is recommended to use CRRT or SLEDD in complicated ARF. (3) The combination of CRRT and iHD is prefer to certain types of ARF such as hepatic encephalopathy, liver transplantation, acute rhabdomyolysis syndrome and hyperbilirubinemia. (4) Whatever which technique choosen, the dialysis adequacy is more important to achieve to correct the endoenvironment disturbance and to improve the renal recovery as soon as possible.

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Different Actions of Inflammatory Mediators and Growth Factors on Tubular Cells (TC): Role in the Recovery from Acute Kidney Injury (AKI) and Potential Diagnostic and Therapeutic Applications

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The number of patients with AKI in ICUs has been sensitively increasing in a clinical setting characterized by injury of TC in presence of sepsis or SIRS. During 2000–2005, we treated about 130 AKI patients/year performing more than 1300 CRRT sessions/year, with a prevalence of 'systemic inflammation' of more than 40%. Basing on these considerations, we evaluated the different effects of inflammatory mediators and growth factors on TC. We previously demonstrated the presence of small peptides in the urine of critically ill patients due to fragmentation of filtered proteins. We have now extended these findings to more than 50 AKI patients confirming that the increase of urinary fragments is mediated by the up-regulation of megalin on TC surface and is an indicator of a 'pre-renal' state. The increased expression of megalin may be related to a sort of defense state against malignant inflammation for maintaining TC viability. However, the prolonged incubation with cytokines or with sera derived from patients with fragmented proteins resulted in alteration of tubular polarity, selective permeability, adhesion to extracellular matrices and triggering of apoptotic pathway throughout Fas and caspases activation. We also studied the key role of TC in the release of different mediators and growth factors that promote de-differentiation, proliferation, migration and tissue repair. Our findings underline the importance of new therapies of blood purification aimed to remove inflammatory mediators, confirm the diagnostic use of fragmented urine proteins and may have potential applications in the engineering of TC or kidney derived stem cells for bioreactors.

Urinary KIM-1 Predicts Severe AKI Earlier than Serum Creatinine in Pediatric Patients

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Acute kidney injury (AKI) is common in critically ill patients (pt) and carries a high mortality. Standard methods of detecting AKI such as serum creatinine (SCr) may not become abnormal until substantial kidney damage has occurred, as recent adult and pediatric study shows 'small' SCr increases (>0.3 mg/dL) are associated with increased mortality. Kidney injury molecule-1 (KIM-1) has been isolated from urine in humans with AKI and is an early AKI marker that precedes SCr changes in small animal models. We prospectively studied critically ill (ventilated and/or receiving 1 + inotrope) pediatric pt to assess if KIM-1 precedes SCr rise in AKI. Daily urine samples were collected on day 1 to 4 of ICU admission for KIM-1 analysis. AKI severity was determined using pediatric modified RIFLE criteria (Risk, Injury, and Failure). The primary outcome was highest RIFLE level achieved by ICU day 14 (RIFLEmax). 102 pt (56 M, 46 F, mean age 5.5 ± 5.9 years) were studied. 44 pt (43%) did not develop AKI (control), 58 patients (57%) developed AKI (R = 42, I = 11, and F = 5). The mean KIM-1 level in the urine on day 1 was 0.28 ± 0.65 in the control group; this level was increased almost 10 fold on day 1 and over 20 fold by day 4 in the RIFLE-F group (see table), one-way ANOVA 3/5 F pt had elevated KIM-1 levels on day 1; all F pt had elevated KIM-1 levels by day 4. Urine KIM-1 excretion preceded rising SCr in 4/5 F pt. Our data support the concept that urinary markers can be used to detect AKI earlier than SCr rise, and hopefully will allow for earlier intervention to prevent worsening AKI and/or lessen mortality/morbidity in critically ill pt with AKI.

	Day 1	Day 4
Control	0.28 ± 0.65	0.20 ± 0.33
Risk	0.29 ± 0.92	0.12 ± 0.41
Injury	0.15 ± 0.35	0.12 ± 0.30
Failure	$2.60 \pm 2.62^*$	$4.46 \pm 6.68^*$

*p < 0.001.

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Evaluation of the RIFLE Criteria in Critically Ill Children with Acute Kidney Injury

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Background: Outcome studies for patients with acute kidney injury (AKI) suffer from lack of a consistent AKI definition. Recently, RIFLE (Risk, Injury, Failure, Loss, ESRD) criteria were proposed to standardize the degree of AKI in adults based on creatinine clearance

and urine output. **Objective:** We prospectively studied a pediatric modified RIFLE in 102 critically ill pediatric (ped) patients (pts) over 7 months to assess (1) AKI incidence and course using RIFLE and (2) if AKI by RIFLE predicted renal function course and/or non-renal comorbidities. **Design/Methods:** See table. **Results:** Mean pt age was 5.5, 5.8, 46 F and 56 M. 44/102 (43%) did not develop AKI, 58 pts (57%) reached R (n = 42), I (n = 11) or F (n = 5). 3 patients (2.9%) required renal replacement therapy as CVVHD and 9 pts died. Severity of illness as measured by Ped Risk of Mortality (PRISM) score was higher for AKI pts (15.2) vs. non AKI pts (11.8, p < 0.05). The majority of AKI patients (60%, n = 35) developed AKI within 7 days of ICU admission. Pts without AKI by RIFLE in the first 7 days were significantly less likely to develop worsening AKI later (2/67 vs. 14/35, p < 0.001; NPV 97%). Pts who developed AKI after 7 days did not progress to F. AKI was not more prevalent in pts with preexisting conditions. Length of stay (hospital and ICU) and mechanical ventilation did not differ for AKI vs. no AKI. **Conclusions:** Our data show (1) a majority of critically ill ped pts develop AKI by RIFLE. (2) Pts who develop AKI do so early in the ICU course. (3) Pts who do not develop AKI early are unlikely to develop severe AKI. We conclude that the RIFLE criteria may serve well to characterize the pattern of AKI in critically ill ped pts. Further study is required to correlate degree of AKI by RIFLE with short and long term pt outcome.

Pediatric modified RIFLE criteria		
	Estimated CrCl	Urine output
Risk	GFR decrease by 25%	< 0.5 ml/kg/hr for 8 hours
Injury	GFR decrease by 50%	< 0.5 ml/kg/hr for 16 hours
Failure	GFR decrease by 75% or GFR < 35 ml/min/1.73 m	< 0.3 ml/kg/hr for 24 hours or anuric for 12 hours

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Renal and Hemodynamic Effects of Intra-renal Nesiritide in Heart Transplant Patients

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Purpose: Inferring the renal effects of drugs in trials of decompensated heart failure using serum creatinine only or retrospective analyses are potentially confounded by a myriad of factors, including concomitant medication use and volume status. Our goal was to determine the actual renal effects of nesiritide (NES), B-type natriuretic peptide, using gold standard methodology and also to assess to what extent the blood pressure lowering effects of NES contribute to its renal effects. **Methods:** We conducted an open-label prospective trial in 10 stable patients post-heart transplant with a history of cyclosporine or tacrolimus use and scheduled for routine left and right heart catheterization. Intra-renal (IR) NES (0.01 mcg/kg/min infusion) was administered for 30 minutes (with (n = 4) or without (n = 6) a 2 mcg/kg IR bolus) via a commercially available bifurcated renal infusion catheter (Benephit Infusion System, FlowMedica) prior to coronary angiography. **Results:** The patients were 3.0 ± 1.0 years post heart transplantation.

The mean age was 56.2 ± 3.9 years, 50% were male, and baseline characteristics included: serum creatinine, 1.4 ± 0.1 mg/dL; serum BNP, 111.6 ± 30.1 pg/mL; ejection fraction $69 \pm 1.2\%$. Systemic exposure to NES, as assessed by plasma BNP levels was significantly higher when NES was administered as an IR bolus (2 mcg/kg) with infusion (0.01 mcg/kg/min) vs. infusion alone ($p = 0.016$). These data suggest that the renal excretion and metabolism of NES can be overwhelmed by a large IR bolus, resulting in greater systemic spillover. IR NES infusion did not affect blood pressure, consistent with a renal first pass elimination effect. In contrast, blood pressure declined following an IR NES bolus. Glomerular filtration rate (GFR, inulin clearance) increased significantly from a baseline of 45.6 ± 2.2 ml/min by $+12.0\%$ within 30 minutes of the start of IR NES ($p = 0.005$). In patients not receiving a bolus, the effects tended to be greater ($+13.4\%$) vs. those receiving a bolus ($+9.9\%$). Renal plasma flow (RPF, para-aminohippurate clearance) increased significantly from a baseline of 297.8 ± 20.2 ml/min by $+16.4\%$ within 30 minutes of the start of IR NES ($p = 0.004$). In patients not receiving a bolus, the effects tended to be greater ($+20.7\%$) vs. those receiving a bolus ($+11.2\%$). Renal vascular resistance declined by 25.6% within 30 minutes of initiation of IR NES ($p = 0.005$). Cardiac hemodynamics were not significantly affected during IR NES infusion in these euvoletic patients. Bilateral renal artery cannulation was rapidly accomplished in all patients (77.5 ± 31.3 seconds) and no procedural complications occurred. There were no drug-related adverse events. **Conclusions:** IR NES safely, rapidly, and significantly increases the GFR and RPF in stable heart transplant patients with renal insufficiency and decreases renal vascular resistance. The fact that RPF increased more than GFR suggests that there is relatively greater afferent than efferent arteriolar dilatation. IR delivery of NES may be a useful strategy for optimizing the drug's beneficial renal hemodynamic effects without causing hypotension. As such, IR NES may prove to be a therapeutic strategy for reversal of renal insufficiency in patients with acute heart failure or those with acute kidney injury in a variety of settings.

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Intra-renal Nesiritide Rapidly and Significantly Improves the Glomerular Filtration Rate and Renal Plasma Flow in Patients with Chronic Kidney Disease Receiving Contrast Media: Data from a Multi-center, Randomized, Placebo-controlled Trial

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Purpose: Previous attempts to demonstrate clinical efficacy of atrial natriuretic peptide in acute kidney injury may have been thwarted by negation peptide's renal vasodilatory effects by dose-related hypotension. We hypothesized that intra-renal (IR) delivery of nesiritide (NES) would both increase renal effects as well as diminish hypotension due to renal first pass elimination of drug, thereby widening the renal therapeutic window. We are conducting a multi-center, randomized, controlled trial to determine the role of targeted

renal therapy with NES in preventing vasoconstriction from contrast media. **Methods:** Patients ($n = 30$) with creatinine clearance < 80 cc/min are randomized 1:1:1 to IV NES, IR NES, or placebo $\times 30$ minutes prior to angiography and during angiography. Glomerular filtration rate (GFR) and renal plasma flow (RPF) were assessed using insulin and para-aminohippurate. The *Benephit* System (FlowMedica), used for simultaneous bilateral drug delivery, is a commercially available device consisting of an 8 F or 5 F sheath through which a bifurcated renal infusion catheter is placed. The 8 F sheath accommodates simultaneous placement of a < 6 F catheter. **Results:** We report interim data from this trial ($n = 16$). Systemic exposure to NES, as assessed by plasma BNP levels, was double when the drug was administered IV vs. IR ($p = 0.03$). RPF increased by a maximum of $+5.4\%$, $+17.0\%$, and $+28.6\%$ in the placebo, IV, and IR NES groups, respectively. From a baseline of 50.5, 49.7, and 55.3 ml/min, respectively, the GFR increased by a maximum of $+7.6\%$, $+18.0\%$, and $+30.0\%$ in the placebo, IV, and IR NES groups, respectively ($p < 0.05$ for IV and IR NES). Despite receipt of a large volume of contrast (~ 260 ml), improvements in RPF and GFR noted during IV and IR NES infusion were maintained at least 2 hours following drug discontinuation. The magnitude of the aldosterone suppression was greater during IR NES than IV NES. Bilateral renal artery cannulation was rapidly accomplished (mean 164 seconds) and no procedural complications occurred in patients receiving the *Benephit* Infusion System. Maximal systolic blood pressure reduction in patients receiving IR vs. IV NES was -10.7 ± 10.1 mmHg vs. -23.7 ± 6.6 mmHg. **Conclusions:** Nesiritide rapidly, robustly, significantly, and safely increases GFR and RPF in vasculopathic patients with chronic kidney disease. The magnitude of these effects is approximately twice as great when the drug is administered IR vs. IV. For example, GFR increased by 30% within 30 minutes of IR NES (0.02 mcg/kg/min). Our data suggest that NES actually has direct renal vasodilatory effects as we have shown that the drug can improve RPF in stable patients with chronic kidney disease who have no reason clinically to have renal vasoconstriction. Compared to IV NES, treatment with IR NES is associated with $\sim 50\%$ lower systemic blood levels and $\sim 50\%$ less systemic blood pressure lowering, consistent with our hypothesis that targeted renal treatment may be able to avert limiting systemic adverse effects of NES. Our data suggest that IR NES may have a role in the treatment and prevention of ischemic acute kidney injury.

Technique Characteristics

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Continuous Veno-venous Hemodiafiltration Therapy for Acute Decompensation with Cerebral Edema in Maple Syrup Urine Disease

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Maple syrup urine disease (MSUD) is caused by an inheritable deficiency in 2-ketoacid dehydrogenase and results in the systemic

accumulation of branched chained amino acids (BCAAs) and their metabolites. During episodes of metabolic decompensation characterized by extremely high serum levels of BCAAs, affected children have severe neurological deterioration often accompanied by life-threatening cerebral edema. Because endogenous renal clearance of BCAAs is limited, therapy has focused on the rapid extracorporeal removal of BCAAs often via intermittent hemodialysis (IHD). However the rapid diffusive clearance of IHD may lead to solute disequilibrium potentially worsening cerebral edema. In this report, a symptomatic 7 year old male with MSUD who developed cerebral edema underwent CVVHD with a small molecule clearance rate of 37.5 ml/min/m². This approach resulted in a nearly 50% decrease in BCAA levels within the first 4 hours of treatment. Therapy was discontinued at 16 hours due to the rapid improvement in neurological status. At that time, serum leucine levels had fallen from 1581 to 268 μ moles/l, isoleucine levels had fallen from 313 to 110 μ moles/l and valine levels had fallen from 652 to 83 μ moles/l. Leucine, isoleucine and valine clearance rates measured during the last four hours of therapy were 30.4, 30.9 and 30.7 ml/min respectively. This case demonstrates that CVVHD is an effective and safe therapy of severe acute decompensation in MSUD accompanied by cerebral edema.

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Application of CRRT without Anticoagulation in Patients with Bleeding Disorders

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Objective: To study the feasibility of continuous renal replacement treatment (CRRT) with non-anticoagulation in critical ill patients with high risk of bleeding. **Methods:** A total of 12 critical ill patients with bleeding diseases requiring continuous renal replacement treatment were prospectively studied. The patients were performed SLEDD (slow low efficient daily dialysis) with total of 28 sessions, the dialyzer were hemophan membrane (GFS Plus-12, Gambro). All circuits received 200mg heparin during rinsing stage for 30–60 minutes. Before connection of the circuit to the patients, the heparin prime was flushed away with normal saline. During SLEDD, no normal saline was returned to the circuits for flushing. The levels of serum creatinine, serum urea, hematocrit, serum

electrolyte and activated clotting time (ACT) before and after CRRT were compared. **Results:** In the 28 SLEDD, the blood flow was 150–200 ml/min, and the dialysate flow was 3000–4000 ml/hr. The ultrafiltration rate was 200–550 ml/hr. The levels of ACT, serum potassium, serum creatinine and urea after CRRT were decreased significantly ($p < 0.01$). But the level of serum sodium, chloride, and bicarbonate were not changed significantly ($p > 0.05$). The spontaneous clotting rate in circuit or in dialyzer was 32.1%. But the mean spontaneous clotting time was 9.15 ± 2.49 hrs. Mean CRRT time was 9.33 ± 2.75 hrs. **Conclusion:** SLEDD without anticoagulation is feasible in patients with bleeding diseases. It is associated with a safe ACT, a satisfactory clearance of toxin and a satisfactory correction of disturbed electrolytes and fluid retention. The circuit longevity is acceptable.

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Dermatan Sulphate: An Alternative to Heparin for Anticoagulation in CRRT

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Dermatan Sulphate (DS) is a natural glycosaminoglycan with a unique mechanism of action on the coagulation system. Unlike heparin, DS selectively inhibits thrombin, does not inhibit Factor Xa, is effective also on fibrin-bound thrombin and does not interfere with platelet functions. To date, no data are available on the use of DS with CRRT. In this work, we compared the effects of both DS and heparin as anticoagulant with patients on CRRT because of acute renal failure complicating cardiovascular surgery. In all patients, CRRT was made according to same protocol: Machine, Gambro Prisma[®]; filter, M100 (AN69, 0.9 m²); QB, 150 ml/min; QD, 2000 ml/hr; QInfusate, 500 ml/min. With 70 CRRT sessions, DS was used as anticoagulant (DS-CRRT): 150 mg bolus at the start, followed by i.v. infusion of 15 ± 4.5 mg/hr. With 93 CRRT sessions, anticoagulation was performed with heparin (H-CRRT): starting bolus of 2000 U, followed by 634 ± 292 U/hr. Blood samples for INR, APTT, Fibrinogen, Hb, PLTS were taken at the beginning of CRRT (Basal) and every 8–12 hours, until the filter clotting. The average value of the blood analyses performed over each session was used for statistics. The duration of each CRRT session represented the filter lifetime, namely, the time measured from CRRT start to filter clotting. There were no differences between DS-CRRT and H-CRRT as far as Basal values of aPTT (44.5 ± 10.8 vs. 41.0 ± 7.5 sec, $p = \text{ns}$), INR (1.40 ± 0.47 vs. 1.49 ± 0.25 , $p = \text{ns}$), Fibrinogen (472 ± 165 vs. 416 ± 152 mg/dl) and Hb (9.3 ± 1.1 vs. 9.7 ± 1.3 g/dl, $p = \text{ns}$) are concerned. Filter lifetime was longer with DS-CRRT than with H-CRRT (49 ± 22 vs. 39 ± 17 hr/session, $p < 0.01$). APTT was shorter through DS-CRRT than through H-CRRT (55.5 ± 10.8 vs. 61.5 ± 19.5 sec, $p < 0.01$). PLTS count did not change through DS-CRRT (144 ± 101 vs. Basal 154 ± 102 , $p = \text{ns}$), whereas lowered through H-CRRT (117 ± 64 vs. Basal 154 ± 92 , $p < 0.01$). In conclusion, DS allowed higher filter lifetime than heparin, together with lower aPTT levels and without significant reduction of PLTS count. These results suggest that DS can be held as a reliable alternative to heparin as anticoagulant for CRRT in patients with high risk of bleeding after major cardiovascular surgery.

Use of Arterio-venous Graft or Fistula in End Stage Renal Disease Patients Receiving Continuous Renal Replacement Therapy

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Continuous Renal Replacement Therapy (CRRT) is increasingly used in end stage renal disease (ESRD) patients with multi-organ failure admitted to intensive care units (ICU). Central venous access is premium in these patients. The present study investigated the use of pre existing arterio-venous (AV) graft or fistula for blood access to perform CRRT in patients with ESRD. The purpose of the study was to evaluate safety and efficacy of the pre-existing AV access in ESRD patients as an alternative to dual lumen catheter for CRRT. **Methods:** The AV access was used in seven ESRD patients for CRRT from Dec. 2004 through Nov. 2005. All patients had AV access cannulated by a dialysis nurse utilizing 14" gauge angio-catheters for arterial access and 16" gauge angio-catheters for venous access. Cannulas were attached to 6' anesthesia extension tubing which was primed with normal saline (NS). Insertion site was covered with a bio-occlusive dressing. Therapy was immediately initiated after cannulation. An ICU nurse was responsible for monitoring, maintenance and unscheduled discontinuation of therapy. The ICU nurses were educated to monitor the AV access on a 1:1 basis and instructed to flush the extension tubing with 10 ml of NS and to clamp the lines in the event that therapy was interrupted. The dialysis nurse was then informed to remove the catheters. **Results:** Seven ESRD patients, 5 males and 2 females with a mean age of 66 years (range 46–76 years) underwent CRRT using AV access. All patients were intubated and were on vasopressors. Blood flow rate was 100 ml/min. PRISMASATE BGK 4/2.5 (Gambro, USA) was delivered at 500 ml/hr as a dialysate. PRISMASATE BGK 4/0 was infused at 1500 ml/hr as replacement fluid. Mean duration of CRRT was 54.75 hours. Citrate anticoagulation was used in 6 (86%) patients. Six (86%) AV accesses were functioning after the CRRT was discontinued. One patient clotted the AV access. No AV access bleeding, infection or technical problems were observed. **Conclusions:** Use of AV graft or fistula with an angio-catheter in ESRD patients receiving CRRT is safe and reduces the need for another central venous access.

Regional Citrate Anticoagulation for Predilutional On-line Hemofiltration

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Introduction: Intermittent predilutional on-line hemofiltration (HF) could have some advantages as a dialysis method for patients in ICU. In these patients regional citrate anticoagulation is frequently required. The aim of our study was to report our experience with citrate anticoagulation for intermittent predilutional on-line HF. **Patients and Methods:** 18 patients with acute renal failure in ICU with active bleeding or high bleeding risk were included in this retrospective analysis.

Patients were 71 ± 10 years old, 12 were male and 6 were female. 37 on-line HF procedures with citrate anticoagulation were performed by our protocol. We used 4% (0.136 mol/l) trisodium citrate infused at the arterial line, on-line prepared infusate with 1.25 mmol/l calcium, lowered sodium (138 mmol/l) and bicarbonate (28 mmol/l) concentrations and 1 M calcium chloride infused at the venous line. On-line HF was performed using Gambro AK-200 Ultra S monitor with individual reverse osmosis. **Results:** Duration of HF treatments was $5\text{ h } 8 \pm 47$ min, infusate volume reached was 78 ± 81 . Dual-lumen or two single-lumen catheters were used for vascular access, locked with 30% citrate in interdialysis period. Average blood flow was 269 ± 52 ml/min, 4% sodium citrate infusion rate was 384 ± 36 ml/h ($2.5 \pm 0.3\%$ blood flow) and 1 M calcium chloride infusion rate was 7.5 ± 1.3 ml/h. None of the circuits clotted. No severe side effects were noted. Ionized calcium was stable during the procedure (1.02 ± 0.16 mmol/l before and 1.13 ± 0.09 mmol/l after HF) as was sodium (141.1 ± 4.8 vs. 143.3 ± 3.5 mmol/l), pH (7.36 ± 0.13 vs. 7.40 ± 0.08 mmol/l) and bicarbonate (24 ± 4.9 vs. 26.3 ± 3.5 mmol/l). **Conclusions:** Predilutional on-line HF with regional citrate anticoagulation using standard, calcium containing infusate (1.25 mmol/l) can be safely performed with good anticoagulation and no severe metabolic derangement.

Machine Generated Bicarbonate Dialysate for Continuous Therapy: A 10-year Experience

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Background: In 1995 we described adapting an intermittent hemodialysis (HD) machine to produce a bicarbonate-based dialysate for use in continuous renal replacement therapies (CRRT). This technique allows for customization of the electrolyte composition of dialysate. Hence, we have almost exclusively supported our acute renal failure (ARF) patients in the intensive care units (ICU) with this dialysate on CRRT in the HD mode. **Objective:** Describe the clinical, biochemical, operational, and cost-related issues involved with self-generated dialysate. **Methods:** We abstracted data from the ARF support registry for patients who developed ARF in the ICU from 1995–2001, and were initially supported with bicarbonate dialysate CRRT. The registry is a prospective, observational cohort study that captured demographic, dialysis therapy, laboratory, and outcome data. All supported ARF patients were recorded from 1995–1998, and then 1 in 5 patients from 1999–2001. We reviewed monitoring tests for the bicarbonate dialysate, limulus amebocyte lysate assays for bacterial endotoxin; and records of CRRT, discarded dialysate, and cost data. **Results:** From 1994–2004, we performed an average of 1353 ± 619 per year of CRRT (1292 ± 587 HD). Dialysate delivery from prescription to patient was 30 min or less for all formulations. There were 405 registry patients. Baseline characteristics: age 59.57 ± 14.41 years, weight 84.2 ± 24 kg, male 65.3%, chronic kidney disease 33.9%, surgery before renal consult 87.9%. 88.4% had veno-venous HD initially and 32.8% switched therapies. 15.1% used heparin. The mean dose of dialysis (ml/kg/hr) for: day 2 was 14.8 (95% CI 14.1–15.5) overall, in males 14.0 (13.2–14.8), in females 16.3 (15.0–17.7); 3-day average was 13.2 (12.6–13.8), in males 12.5 (11.9–13.1), in females 14.5 (13.3–15.6). The mean dose was

higher in 1999–2001 than 1995–1998. Serum sodium, potassium, calcium, magnesium, phosphate, and bicarbonate concentrations were well-maintained. 55 ± 29 bags were discarded per month; 7% from prescription change, 62% expiration at 72 hours, 6% stopped CRRT, 24% bag leak. No random dialysate monitoring test was positive. No dialysate related complications or reactions were reported. Total cost per liter (materials + labor) in 1995 was \$0.91 and \$0.67 in 2005. **Conclusion:** ICU patients with ARF can be supported on CRRT-HD mode with machine generated, and customized, bicarbonate-based dialysate.

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Vascular Access in Critically Ill Patients with Acute Renal Failure Treated with Hemodialysis/Hemofiltration

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The purpose of this retrospective clinical study was to evaluate complication rate of hemodialysis (HD) catheters which have been inserted between January and October 2005 as acute vascular access in critically ill patients with acute renal failure having been treated with HD. **Patients and Methods:** In 84 critically ill patients, 59 men, 25 women, aged from 36 to 92 years (mean 68 ± 11), totally 155 HD catheters have been inserted: 89 single lumen, 55 double lumen into femoral vein; 2 single lumen, 6 double lumen into jugular vein; 1 single lumen, 2 double lumen into subclavian vein. Real time ultrasound guidance was used for the insertion of jugular/subclavian catheters. Mupirocin ointment was applied at the exit site. Single lumen catheters were primed with 4% and double lumen with 30% trisodium citrate. **Results:** Catheters were inserted for totally 1722 days and 1137 HD have been performed. Insertion was free of complications. In 36/155 (23.2%) catheters the following side effects were observed: 30 (19.4%) catheters had to be removed and replaced over a guidewire (thrombosis of the lumen in 17 catheters /11.1%, thrombosis of the vein in 1 catheter /0.6%, mechanical damage in 5 catheters /3.2%, avulsion in 3 catheters /1.9%, suspected exit site infection in 2 catheters /1.3% and suspected catheter related septicemia in 2 catheters /1.3%), in 3 (1.9%) r-TPA was applied for thrombolysis, and in 6 (3.9%) flushing with saline and transient change in blood flow direction reversed malfunction (low blood flow). Overall complication rate was 20.9/1000 catheter days. Complication rate for single lumen catheters (10.7/1000 catheter days) was significantly lower vs. double lumen (24.4/1000 catheter days) ($p < 0.05$). Complication rate for single lumen femoral catheters (11/1000 catheter days) was significantly lower vs. double lumen femoral catheters (24.4/1000 catheter days, $p < 0.05$). Overall complication rate of femoral catheters compared to subclavian and jugular catheters was not significantly different (15.6/1000 vs. 16.8/1000 catheter days, $p = 0.92$). There were 1.16 exit site infections/1000 catheter days and no catheter related septicemia. **Conclusions:** Significantly higher complication rate was observed in double lumen catheters. No difference was observed in complication rate between femoral and subclavian/jugular catheters.

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CRRT in Leptospirosis in Developing Countries

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Leptospirosis is an important cause of acute renal dysfunction in southern parts of Kerala which is a state in South India. Leptospirosis causes multiorgan dysfunction with involvement of kidney, liver, heart and blood components with hemodynamic instability being very common. In our study, we attempted to define the role of CRRT in altering the outcome in patients with leptospirosis and hemodynamic instability. All patients with clinically suspected leptospirosis admitted to Medical College Hospital, Trivandrum from January 1, 2003 to December 31, 2004 were taken for the study. Patients who underwent CRRT for less than 6 hours were excluded. There were 22 patients in the study group with a mean age of 46.9 ± 15.4 years. Male to female ratio was 3.4:1. All patients had multiple organ involvement. 12 patients (54%) required more than one sitting of CRRT. CVVHDF was the most common modality of CRRT employed. 63.6% patients survived. Follow-up of these patients at 6 weeks showed normal renal, liver, cardiac and hematological parameters. We conclude that CRRT remains an important modality of renal support in patients with leptospirosis with renal involvement and multiorgan dysfunction in developing countries. The limitations to the administration of CRRT were the patient's financial constraints which necessitated the use of PD fluid (which was prepared inside the hospital) as dialysate fluid, the use of F8 filter instead of CVVH filter and the lack of facilities for continuous monitoring of biochemical parameters and blood gases. We also used an ordinary blood pump instead of sophisticated CRRT equipment available in developed countries.

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Implementation of 35 ml/kg/h of CRRT Dose in ICU: A Combined Medical and Nursing Approach

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Objectives: Describe all the rigorous education process performed inside the nursing and the medical team in order to make possible this change from 20 ml/kg/h up to 35 ml/kg/h. **Background:** In early 2002, we decide to implement 35 ml/kg/h as a standard dose of CRRT in all our patients according to the study of Ronco publish in the lancet 2001. For the past 15 years, we have been using CRRT with BSM 22, BM 25, Prisma and finally Aquarius. A nursing cell specially dedicated to CRRT has been created in our unit more than ten years ago. This cell allow us to have dedicated nurses to CRRT in every shift. This is very helpful also when we do need to implement new machines or

new techniques. Such a change need a rigorous education process in the nursing cell first and than to the whole nursing team as well physicians including colleagues. **Setting:** General Hospital, Regional Centre of 450 beds, Interland population of 150,000 inhabitants and a medical-surgical general ICU of 15 beds having 1000 admissions a year. The Unit is performing from 40 CRRT patients up to 50 CRRT patients per year. **Design:** Descriptive study and reported single centre experience. **Changes Made in the Daily Practice:** (1) Vascular Access: need of a co-axial catheter of 14 french. The catheter site had to be exclusively a Right internal Jugular Approach (Posterior one) with a 20 cm length and the tip of the catheter placed in the right atrium. Indeed, in order to perform 35 ml/kg/h in each patient regardless of the body weight (from 50 kg up to 150 kg), we need a blood flow of 300 ml/min in order to keep the filtration fraction around and below 30%. Indeed for a 50 kg patient = $35 \times 50 = 1,750$ l/h which gives an FF of less than 15% but for a 150 kg patient = $35 \times 150 = 5,250$ l/h, this gives an FF of 29%. You can obviously not keep changing your blood flow upon the body weight of the patient. You need to stick to very strict rules. The choice of the RIJ approach need a very large consensus within all the ICU consultants and again very strict rules have to be applied. (2) Pre- and Post-Dilution Policy: according to the latest literature, we did choose 33% of pre-dilution and 66% of post-dilution. This policy allow us to prevent some clotting and some clogging by the use of a certain amount of predilution. This policy also permits to sustained a good convection rate. Indeed, the loss of convection by the concomitant use of pre-dilution reduces the risk of fouling and protein cake formation and finally preserve further loss of convection. (3) Pre-determination of the Exchange rate according the body weight: in order to reduce the workload at the beginning of the CRRT, we did introduce full tables which can give automatically the amount of pre- and post for a given body weight eliminating the need of sophisticated calculation that can lead to further mistakes. Additional tables do exist also regarding the adaptation of antibiotics to 35 ml/kg/h and other drugs as well. (4) No further need of associate dialysis: during the last three years, even in very severe rhabdomyolysis cases, no need of associate dialysis was required whatever the release of potassium was. This allow us to use the aquarius with combined pre-and post-dilution and also to save money regarding additional cost of fluids. **Conclusions:** This descriptive and reporting study is showing that the implementation of new guidelines as the 35 ml/kg/h rule can not be decided in one day. This will need a rigorous longstanding educational process as well for the nursing staff and for the medical team. A nursing cell can be of help in order to achieved this. We will embark soon upon the implementation of citrate using the same implementation and educational process.

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Efficacy and Safety of Regional Citrate Anti-coagulation in High-flow CVVH

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Purpose of the Study: Continuous Renal Replacement Therapy (CRRT) improves critically ill patient's survival when ultra-filtration (UF) exceeds 35 ml/kg/h. This study evaluated the safety and efficacy of citrate regional anti-coagulation in high dose continuous veno-venous hemofiltration (CVVH). **Methods Used:** We initiated a new high

flow CVVH protocol utilizing citrate for regional anti-coagulation in September 2004. After our new protocol had been used for a year, we randomly chose two consecutive months to retrospectively evaluate the efficacy and safety of our newly implemented citrate anti-coagulation protocol. Patients were placed on the NxStage system one (NxStage Medical, Lawrence, MA) with a blood flow (Qb) of 250 ml/min and replacement fluid (Qrf) rate of 3 liters/hr. The primary renal team adjusted Qb and Qrf as clinically deemed appropriate. The primary endpoint was filter life. Secondary endpoints included UF rate, electrolyte abnormalities, and citrate toxicity. Laboratory values were followed every 8 hours while on citrate anti-coagulation including sodium, bicarbonate, BUN, creatinine, total calcium as well as serum and post filter ionized calcium levels. **Summary:** 56 systems (filters) utilizing citrate anti-coagulation and 12 systems (filters) utilizing standard heparin anticoagulation in a total of 19 patients were evaluated. Patients developed renal failure from multiple causes. The citrate systems and heparin systems average filter lives were 33 hours and 24 hours respectively ($p = 0.09$). After censoring for interruption due to procedures, catheter failures, expiration of the patient or system no longer needed, there were a total of 39 systems with citrate anti-coagulation and 9 systems with heparin anticoagulation. The average filter life of the citrate vs. heparin system was 40 hours vs. 31 hours ($p = 0.09$) respectively. The average UF rate was 49 ml/kg/min. There were no cases of citrate toxicity. Review of electrolyte safety revealed one incidence of metabolic alkalosis, one incidence of hyponatremia, one incidence of hypokalemia, one incidence of hyperkalemia. No incidences of hypernatremia occurred. **Conclusions:** Citrate anti-coagulation for high-flow CVVH is safe and efficacious. The filter life is prolonged vs. heparin anticoagulation. Electrolyte abnormalities are minimal with frequent surveillance. There were no cases of citrate toxicity, despite several patients with advanced cirrhosis.

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Citrate Anticoagulation for Fresenius CRRT

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Purpose of Study: Regional extracorporeal anticoagulation with continuous citrate and calcium chloride can be performed easily, safely and is efficacious. We describe our protocol for this technique and summarize our results for the previous year. **Methods:** Demonstrate our program and discuss implementation results. **Summary:** CRRT with this system has been done at our institution since April 13, 2002. A dialysis RN does the initial setup, a daily assessment and is the support person for the ICU/CC (intensive care unit/critical care) RN doing the CRRT treatment, along with the supervising nephrologist. Citrate is run continuously into a Y connect at the catheter hub, into the CRRT system and calcium chloride into a Y connect at the venous catheter hub, or through a separate central line if systemic anticoagulation is prescribed. A zero calcium dialysate is used. Monitoring with ionized calcium levels and a sliding schedule for the calcium chloride drip is used by the RN. Ease of use, problem solving, calls, and safety issues will be discussed. CRRT was performed on 71 patients between October 2004 through September 2005 for 617 CRRT 24 hr treatments. **Conclusion:** Citrate anticoagulation with the Fresenius CRRT system is efficacious, relatively simple and safe to use.

Table for Abstract 35

# Pts	Days on CRRT	Tech prob	Bleeding prob	Cath changed	Yeast in drain	SUN mg/dl	eGFR on CRRT
30	<5	No	No	No	Rarely	<20	30–70
31	5–10	No	No	No	Periodic	<20	30–90
9	10–20	No	No	Yes	Periodic	<20	>90
2	20–30	No	No	Yes	Periodic	<20	>90
1	30–40	No	No	Yes	Periodic	<20	>90
1	50–60	No	No	Yes	Periodic	<20	>90

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Fresenius CRRT for Extended Critical Care Treatment Support

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Purpose of Study: CRRT for the unstable patient in critical care. We describe our protocol for this technique and summarize our results for the previous year. **Methods:** Demonstrate our program and discuss implementation results. **Summary:** CRRT with this system has been done at our institution since April 13, 2002. A dialysis RN does the initial setup, a daily assessment and is the support person for the ICU/CC (intensive care unit/critical care) RN doing the CRRT treatment, along with the supervising nephrologist. Over the period of 12 months from 10/01/2004 through 9/30/2005 we had 71 patients on CRRT 24/7 for extended treatment each listed as days, and a total of 617 treatments for the year. **Conclusion:** Extended periods of CRRT can be done to maintain fluid balance and control uremia.

with 4 mEq/L potassium and 2.5 mEq/L calcium was used for 97% of total doses (517/535). In the historical control group, 26 different combinations of pharmacy made dialysate solutions were used in 20 patients. Ready to use dialysate plus electrolyte replacement protocol led to a decrease in percentage of time patients spent with potassium <3.5 mmol/L as compared to pharmacy made dialysate solution (10.7% vs. 18.3%). There was a reduction in rate of potassium replacement doses (0.026 vs. 0.033 replacements/hr). Nursing satisfaction with ready to use dialysate was very high. The nurses survey revealed a perceived improvement in workflow (33/41), in patient care (31/41), and a sense that the ready to use dialysate was a positive change (38/41). Cost analysis (material plus labor) showed that pharmacy made dialysate was significantly more costlier than ready to use dialysate solution. **Conclusions:** Our evaluation of ready to use dialysate plus electrolyte replacement protocol showed to be effective in managing electrolyte balance, reduced the number of electrolyte replacement doses, decreased pharmacy workload, and resulted in a perception of increased nursing time for patient care, thereby serving as potential means to reduce error. In addition, the change offered an anticipated cost savings.

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Ready to Use vs. Pharmacy Made Dialysate Solution for Continuous Renal Replacement Therapy

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Purpose of Study: To evaluate the utility of ready to use dialysate in place of pharmacy made dialysate solutions for CRRT with particular attention to electrolyte balance, electrolyte replacement, workload of pharmacy, nursing workflow, and impact on cost. **Method:** An evaluation of ready to use dialysate solutions was conducted at the Ohio State University Medical Center. Data was collected on 24 patients for whom ready to use dialysate and electrolyte replacement protocol was used. Data collection included: ready to use formulation (4 formulations available), hours on CRRT, electrolyte levels, and hours above or below target electrolyte range. This data was compared to an historical control group of 20 patients. A survey was distributed to MICU/SICU nurses (n = 41) to collect their opinion on the use of ready to use dialysate solutions. An economic evaluation of ready to use and pharmacy made dialysate was completed by a Value Analysis Facilitator. **Results:** Ready to use dialysate formula

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A Technique for Rapid Exchange of a Continuous Renal Replacement Therapy

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Re-initiation of continuous renal replacement therapy (CRRT) in neonates and young infants weighing less than 15 kilograms often necessitates a blood prime of the blood circuit path or a concurrent packed red blood cell (PRBC) transfusion to avoid causing hemodynamic instability due to acute hemodilution. The significant amount of time required for a routine CRRT circuit change can be associated with worsening electrolyte and acid-base abnormalities, fluid retention, fever, greater hemodynamic instability and reducing effective hemofiltration time. In an attempt to limit the time without CRRT and to eliminate the requirement for additional blood exposure, a new technique, rapid exchange of CRRT (RECRRT), was developed. Rapid exchange of CRRT is a sequential technique which transfers citrated blood from one CRRT machine to another machine connected in

series. The technique effectively negates the requirement for CRRT circuit path blood priming or PRBC transfusion. The amount of time without CRRT is markedly reduced by RECRRT to 2–3 minutes. The RECRRT technique has been utilized more than 30 times for 15 patients without an adverse event. RECRRT may benefit children who weigh less than 15 kilograms and in those patients who experience hemodynamic or clinical instability while CRRT is discontinued for only a brief period.

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Calciophylaxis Treated with Sodium Thiosulfate and Continuous Veno-venous Hemofiltration (CVVH)

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Purpose: To report a case of calciophylaxis treated with sodium thiosulfate and CVVH. **Material and Methods:** A 79-year old woman was admitted after developing hypotension following hemodialysis. Hemodynamic support was required and antibiotics were initiated. An area suggestive of calciophylaxis was present on the abdominal pannus characterized by a large band-like area of painful indurated necrosis without ulceration. Intravenous sodium thiosulfate and intermediate hemodialysis (IHD) was initiated, followed soon thereafter by CVVH with an ultrafiltration rate of 3 L/h. She was subsequently converted to IHD with sodium thiosulfate. After an additional 3 IHD/sodium thiosulfate treatments, she was discharged. The area of calciophylaxis was painless, less indurated and erythematous, and without ulceration. IHD and sodium thiosulfate were continued. Twenty-four days later she was found to have painful, weeping non-healing ulcers and was readmitted. Surgical consultation was obtained, and she was treated with antibiotics, IHD and sodium thiosulfate. She expired 10 days later after the family elected comfort care. **Discussion:** Calciophylaxis is a life-threatening condition that occurs in approximately 1% of chronic renal failure patients. The mortality rate is approximately 30% in those without ulceration, but, approaches 80% once ulceration is present. Although the pathogenesis had not been fully elucidated, it is believed that vascular calcium deposits play a role. As such, treatment has focused on the reduction in levels of serum calcium, phosphorous and their product. Other recommendations have included the use of a low-calcium dialysisate, cessation of calcium-containing phosphate binders and vitamin D supplements, parathyroidectomy, and the use of prednisone if ulceration is not present. Recently, intravenous sodium thiosulfate has shown promise. Thiosulfate is extremely soluble and is believed to allow the dissolution of insoluble calcium salts. Once mobilized, these salts are cleared by CVVH. **Conclusion:** It is unclear whether combination or individual therapy resulted in initial improvement. However, given that her lesions were non-ulcerative at the time of discharge but severely ulcerative after 3 weeks of IHD with sodium thiosulfate suggest CVVH may play an important role. Future study is needed to elicit whether one modality or its combination is of most benefit.

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Safety of 0.5% Isotonic Citrate Replacement Solution for Continuous Venovenous Hemodiafiltration (CVVHDF)

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Purpose: While commercial citrate solutions are approved for blood bank applications, there are currently no FDA-approved citrate solutions for CRRT. Furthermore, available citrate solutions in the U.S. are concentrated and hypernatremic. Use of an isotonic, dilute citrate solution offers two distinct advantages in CRRT: (1) a lower incidence of hypernatremia; and (2) a minimal risk of citrate-related metabolic complications with higher infusion rates. This study reviews the safety of a 0.5% isotonic citrate solution delivered as replacement fluid with commercially available dialysates in CVVHDF. **Methods:** A retrospective review of patients undergoing CRRT from May 2004–October 2005 at a tertiary center was performed. Data collected included demographics, clinical parameters, diagnosis, renal failure etiology, chemistries, arterial blood gas, coagulation indices and CRRT parameters. Up to 7 days of data following CRRT initiation were analyzed. Primary markers for citrate toxicity were a total calcium/ionized calcium (Ca/iCa) ratio >2.5 and serum ionized calcium (iCa) <0.8 mmol/L. The primary marker of hypernatremia was serum sodium (Na) >150 mmol/L. Secondary markers for citrate toxicity included bicarbonate (HCO_3^-) >30 mmol/L and pH >7.5 . **Results:** Of 413 patients treated with CRRT using 0.5% citrate, the first 100 were reviewed. Mean age of this cohort was 57 ± 17 years, and 35% were female. Of the 100 patients, 8% had known cirrhosis at CRRT initiation. Causes of renal failure included: sepsis (30%), surgery (14%), hypoperfusion (11%), multifactorial (11%), drug-induced (9%), ESRD (9%), cardiogenic (8%), hepatorenal (4%), and other (4%). At CRRT initiation, mean patient weight was 91 ± 23 kg, mean dose of dialysis was 33 ± 7 ml/kg/h, and mean effluent rate 2877 ± 738 ml/h. An average of 5 days of data per patient was available for analysis. 90% of patients had no citrate toxicity as per the two primary markers, and only 3% (2%-cirrhosis, 1%-cardiogenic) had citrate toxicity as per abnormal values for both primary markers. Of patients with both abnormal iCa and Ca/iCa levels, only 2 had cirrhosis, and neither required discontinuation of citrate therapy. 8% of patients developed iCa <0.8 mmol/L (mean iCa 0.74 mmol/L), and 10% developed Ca/iCa >2.5 (mean 2.70). 4% of patients had Na >150 mmol/L (peak Na 153 mmol/L). In terms of secondary markers, 22% had a pH >7.5 (7.51–7.60), while 7% had $\text{HCO}_3^- >30$ mmol/L (peak HCO_3^- 33 mmol/L). However, just 2% had both abnormally elevated pH and HCO_3^- levels. There were no adverse events directly related to 0.5% citrate. **Conclusion:** Nearly all patients who received 0.5% isotonic citrate for CRRT had favorable biochemical profiles during the study period. Preliminary data from this ongoing study suggest that 0.5% isotonic citrate is a safe and promising option for use as a standardized citrate solution in CRRT therapy.

Table 1 for Abstract 40

	2 L/hr		3 L/hr		4.5 L/hr	
	Urea	B2M	Urea	B2M	Urea	B2M
NxStage CVVHD	30.9 ± 2.9	20.5 ± 8.4	48.0 ± 2.0	20.6 ± 2.8	75.2 ± 2.6	23.7 ± 6.5
Prisma/M100 CVVHDF*	31.7 ± 0.9	14.5 ± 1.6	46.6 ± 1.3	15.2 ± 2.0	60.6 ± 2.6	20.5 ± 4.3

* For Prisma CVVHDF 2 L = 1 L HD, 1L HF; 3 L = 2 L HD, 1L HF; 4.5 L = 2.5 L HD, 2 L HF.

Performing CVVH at 3 L/hr with the NxStage machine yielded urea clearances of 45.3 ± 0.8 and B2M clearances of 19.2 ± 4.3 ml/min.

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Improved Diffusive Solute Clearances with Novel CRRT Equipment and Dialyzer Design

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Purpose: Continuous veno-venous hemodiafiltration (CVVHDF), a combination of diffusive and convective therapies, is a commonly practiced modality that achieves high small solute and middle molecule clearances within the cost and regulatory constraints of fluids for direct infusion. We hypothesized that higher clearances of small solutes and middle molecules could be achieved during purely diffusive therapies when using large surface area dialyzers containing membranes with improved clearance capabilities. This study determined small solute and middle molecule clearances at flow rates consistent with critical care applications using the NxStage System One (NxStage Medical) with its next generation membrane technology (PUREMA, 1.46 m², Membrana GmbH) and compared these findings to CVVHDF as conventionally administered. **Methods:** Clearances were determined for urea and beta-2-microglobulin (B2M) during purely diffusive (CVVHD) therapy from blood and effluent sampling in an *in vitro* bovine blood model after the addition of urea and human B2M. Blood flow rates were 250 mL/min. CVVHD dialysate flow rates were 2, 3, and 4.5 L/hr. Additional studies were also performed during predilution hemofiltration (CVVH) with a replacement fluid flow of 3 L/hr. Net ultrafiltration was zero; four tests were performed under each condition using 4 separate dialyzers. Experimentally determined clearances were compared to those published previously (Brunet et al, AJKD 1999) using the Gambro Prisma and M100 cartridge. **Results:** Determined mean ± SD clearances (in mL/min) for urea and B2M were as follows in table 1. **Conclusions:** Urea clearances (at 3 & 4.5 L/hr) and B2M clearances (at 2, 3 & 4.5 L/hr) are higher with the NxStage system in a purely diffusive (CVVHD) mode than during CVVHDF as conventionally administered. These results are achieved in a simpler format (only one source of fluid) and with lower patient exposure to pharmacy compounding or contamination risk.

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Pediatric Plasma Exchange during Extracorporeal Membrane Oxygenation: Electrolyte and Coagulation Monitoring

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Purpose: Describe the technical aspects and laboratory results of performing therapeutic plasma exchange (TPE) in a 5 year old (22 kg) male on extracorporeal membrane oxygenation (ECMO).

Methods: This patient was 10 months post cardiac transplant for hypoplastic left heart presented with heart failure. He rapidly deteriorated and was initiated on VA-ECMO for cardiac failure secondary to antibody mediated rejection. TPE was initiated to reduce antibody levels. The patient was maintained on pulse methylprednisolone, cyclosporine and mycophenolate mofetil, with dosing supplementation based on anticipated TPE treatment reductions in these drugs. The PRISMA (Gambro) with TPE 2000 filter (Gambro) was used. Arterial access was connected pre-ECMO bladder via a high flux stop-cock and venous return was to the ECMO bladder. Blood flow rate was 100 mL/min (4.5 mL/kg/min). The patient received 6 separate one volume plasma exchanges (3000 mL total volume) at 500 to 1000 mL/hr. Patient's total blood volume was 1540 mL (70 cc/kg) and ECMO circuit volume was 2000 mL (estimated patient plasma volume 1043 mL). Calcium chloride (CaCl₂) infusion (20 mg/mL) was initiated at 7 mL/hr, but increased to 14 mL/hr (0.6 mL/kg/hr) during TPE + ECMO. Replacement fluid aliquots were: 250 mL 5% albumin alternating with 250 mL fresh frozen plasma (FFP) for a total of 1500 mL 5% albumin and 1500 mL FFP. **Summary:** PRISMA arterial and venous pressures remained between -179 to -233 mmHg and 71 to 181 mmHg, respectively. The trans-membrane filter pressures ranged from 21 to 39 mmHg. CaCl₂ drip was initiated for concerns of hypocalcemia from FFP containing citrate and calcium depleted 5% albumin. Initial ionized calcium was 1.11 mEq/L, but follow-up ionized calcium after 30 minutes of therapy and 250 cc of 5% albumin replacement was 0.96 mEq/L. This occurred once and after increasing the calcium infusion rate to 14 mL/hr the ionized calcium remained normal (1.10–1.22 mEq/L) for the remaining 6 treatments. Hypokalemia and hypomagnesemia occurred during TPE and required frequent monitoring and replacement. A contributing factor was secondary diuresis from furosemide (0.1 mg/kg/hr), but both electrolyte levels decreased during TPE+ECMO. PT/INR, PTT and fibrinogen results remained within clinical parameters. **Conclusion:** TPE in patients on ECMO is technically feasible and can be

performed without complications. Our experience supports the need for close follow-up of electrolytes in these patients.

Table 1. Representative Lab Results of a Single Pre-, Intra- and Post-TPE Treatment:

Labs	Pre-TPE	Intra-TPE ^a	Post-TPE
Ionized calcium (mmol/L)	1.14	1.12	1.20
Potassium (mEq/L)	3.8	4.6 ^b	3.2
Magnesium (mg/dL)	2.1	1.8	1.7
Sodium (mEq/L)	144	—	145
Phosphorous (mg/dL)	4.4	—	3.6
Creatinine/BUN (mg/dL)	2.4/104	—	2.2/92
Albumin (g/dL)	3.2	3.0	3.2
Hematocrit (%)	29.3	—	35.1
PT/INR (sec)	12.9/1.3	13/1.3	14.2/1.5
PTT (sec)	78.4	60.2	79.5
Fibrinogen (mg/dL)	156	162	133

^a2 hrs/1.5 L exchange.

^bpost-replacement 1 mEq/kg KCl.

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Clipped Single-bag Development for Bicarbonate Replacement Fluid

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A new clipped single-bag type bicarbonate replacement fluid set has been developed. In the recent past, double-bags with bicarbonate replacement fluid have been used for hemofiltration and hemodiafiltration. However, caregivers sometimes forget the proper mixing procedure (compressing the bag to break the inner seal separating the two solutions or snapping the inner cap of the bag). This may produce imbalance of electrolyte and acid base. In order to resolve this problem, we have developed a single-bag with a clip. The bag consists of two inner chambers that separate the solutions. The use of this bag is extremely simple and mishap free. When the caregiver is ready to administer treatment, the bag is simply unfolded and the clip automatically detaches, releasing the fluids; thereby, the fluid is accurately mixed and ready to administer to the patient. This design eliminates the additional mixing step necessary which is sometimes overlooked with previous bag designs. In this study the clipped single-bag pressure resistance and shock resistance were tested using different clip sizes. An optimal clip size was with an outer diameter of 16 mm and thickness of 2 mm. This new clipped single-bag type bicarbonate replacement fluid set will effectively establish proper mixture of the bicarbonate automatically.

CRRT Research

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Animal Experiments of Pulsatile Blood Flow for Hemofiltration

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Although the daily home hemodialysis treatment has many clinical efficacies over the conventional intermittent hemodialysis, huge water treatment facility has been a main obstacle to home dialysis. Because the hemofiltration treatment employs several simple replacement fluid bags without huge water treatment facility, some researchers said daily hemofiltration treatment could be an alternative for daily home hemodialysis. In this study, the animal tests were performed in dogs to evaluate the high convection effects of the pulsatile blood flow in reducing the required water requirements in hemodiafiltration. The results show that the use of pulsatile blood flow can preserve the efficiency of dialyser or hemofilter, and reduce the total water volumes. Pulsatile blood flow can retard the reduction of total cell volume by decreasing the protein adsorption on the semi-permeable membrane. We are developing the daily home hemofiltration system integrated with pulsatile blood pumping mechanism. Pulsatile blood pumping mechanism is transferred from artificial heart's pump technology which is free from hemolysis and thrombosis problems, and its flow rate is modified suitable to renal replacement therapy. We expect the daily home hemofiltration therapy using pulsatile-flow pump to complement the inconvenience of in-center hemodialysis and to improve the quality of life of patients.

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High Volume Hemofiltration in the Management of Severe Hyperdynamic Septic Shock

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Introduction: Early mortality in septic shock is usually due to refractory hypotension and progressive acidosis unresponsive to fluids and vasopressors. High-volume hemofiltration (HVHF) could have a role in this setting. Experimental and clinical studies suggest a beneficial effect of HVHF in severe hypodynamic septic shock. Nevertheless, the most prevalent condition is hyperdynamic (75% of cases) in which high cardiac output and low systemic vascular resistance are present. There are no studies specifically addressing the effect of HVHF in severe hyperdynamic septic shock. Our aim was to

Table 1 for Abstract 44

		T0	T4	T8	T12	T18	T24
NE (ug/k/min) NE (ug/k/min)	R	0.72 ± 0.5	0.43 ± 0.3*	0.27 ± 0.2*	0.16 ± 0.2*	0.09 ± 0.1	0.05 ± 0.1
	NR	0.78 ± 0.5	0.63 ± 0.6	0.56 ± 0.4	0.4 ± 0.2	0.42 ± 0.2	0.35 ± 0.2
Lactate (mEq/L)	R	5.7 ± 3.4	4.3 ± 2.9	3.61 ± 2.1*	3.59 ± 2*	3.2 ± 1.9	2.84 ± 1.7
	NR	5.6 ± 2.7	6.4 ± 3.7	7.54 ± 3.4	7.53 ± 3.2	7.92 ± 3.6	7.9 ± 3.8
MAP (mmHg)	R	71.8 ± 8.7	84.2 ± 9*	81.4 ± 6	79.1 ± 4.5	78.5 ± 9	78 ± 8
	NR	72.8 ± 14	73.2 ± 5	69.4 ± 13	69.8 ± 8	74.1 ± 10	77 ± 12

assess the effect of short-term (12 h) HVHF on norepinephrine (NE) requirements and lactate levels in patients with severe hyperdynamic septic shock. We also compared expected vs. observed ICU mortality.

Methods: A prospective, interventional, non-randomized study was carried out in surgical and medical intensive care units of an academic tertiary centre. We included twenty consecutive patients with severe septic shock, previously unresponsive to a full evidence based-management algorithm and with increasing NE requirements (>0.3 ug/k/min) and lactic acidosis. The intervention was a single-session of 12 h HVHF. We measured changes in NE requirements and perfusion parameters every 4 h during HVHF and 6 h thereafter.

Results: Mean baseline NE dose was 0.76 ± 0.5 ug/kg/min and it decreased significantly by 33% at 4 h, 43% at 8 h, and 63% at 12 h. Fourteen patients decreased NE requirements and 11 of them decreased lactate levels (responders = R). Nine patients did not decrease NE requirements (non-responders = NR) within 12 h. Table 1 shows the differences found between R and NR compared to baseline (T0; * = $p < 0.05$). Severity scores predicted ICU mortality rate in 60%, significantly higher than the observed 40%, being concentrated in NR (83% vs. 21%, $p < 0.001$). **Conclusion:** This is the first clinical study in patients with severe hyperdynamic septic shock, treated with HVHF according to an evidence-based management algorithm. It confirms that HVHF may significantly improve hemodynamic and perfusion parameters. A positive effect on mortality it is also suggested.

tracked daily and all data were analyzed using ANOVA for repeated measurements. Patients were defined as hemodynamic responders if catecholamine doses required decreased more than 50% with hemodynamic improvement. Comparison between expected vs. observed mortality was made by a CHI2 test. **Results:** The mean SAPS II was $65 (\pm 9)$ and mean age was 60 years (± 15). The global observed mortality was 50% vs. an expected mortality of 77% ($p < 0.05$). Twenty three patients were hemodynamical responders with a mortality of 17% and 15 were not and all died. Responders and non-responders characteristics (SAPS II, age, organ failure...) were comparable at the beginning, excepted the weight, because the responders were significantly lower in body weight (70 vs. 85 kg). All the parameters (hemodynamic and biologic) improved in the responders group while non-responders had more hepatic failure. **Discussion:** Observed mortality was significantly better than the expected one. Hemodynamic improvement has a good prognostic value in term of survival. The weight is an important parameter, not only for the hemofiltration dose adaptation but perhaps also for the specific inflammatory status in the overweight population which could explain the hemodynamic response difference. In the previous study, all the patient were responders with HVHF (50 ml/kg/h) maintained during 96 hours. PHVHF is more practicable but could be perhaps less effective than maintained continuous HVHF.

Reference

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'Pulse' High Volume Hemofiltration in Septic Shock

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Introduction: The purpose of this study was to evaluate the effect of 'Pulse' High Volume Hemofiltration (PHVHF) on hemodynamics and outcome in patients with septic shock. The primary end point was the mortality at 28 days, secondary end point was hemodynamic and organ failure evolutions and at last the comparison with previous study [1]. **Materials and Methods:** Prospective study in two centers (France and Belgium) in which 38 patients with septic shock were included. All patients were treated by PHVHF with ultrafiltration rate of 100 ml/kg/h for 4 hours and 35 ml/kg/h the next 20 hours. Changes in hemodynamic variables and doses of norepinephrine required were measured regularly and the biological parameters were

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Hydroxypropyl Beta Cyclodextrin Transmembrane Clearance during in vitro Continuous Venovenous Hemofiltration (CVVH)

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Objectives: Cyclodextrins are cyclic oligosaccharides used to increase solubility of lipophilic drugs, improve bioavailability, resist degradation, or enhance safety profile. 2-Hydroxypropyl beta cyclodextrin (HP-CD) is used in several marketed agents including intravenous and oral itraconazole solutions and an investigational antibacterial agent, telavancin. HP-CD is primarily renally eliminated, therefore its use is not

recommended in renal failure. It has a large molecular weight which suggests that it may not be removed by renal replacement therapy yet its small volume of distribution (~18 L) suggests that it may be removed by CVVH. Clinicians using drugs containing HP-CD have concerns about HP-CD accumulation, however, there are no published data regarding HP-CD disposition in CVVH. The objective of this study was to determine CVVH HP-CD transmembrane clearance (CI) with two commonly used hemofilters at conventional ultrafiltration (UF) rates. **Methods:** HP-CD CI was assessed in our validated in vitro CVVH model using citrate anticoagulated, bovine blood and a B. Braun Diapact machine. Telavancin coupled with HP-CD was added to blood and experiments were run using new AN69 (M100, Gambro) and polysulfone (F160NR, Fresenius) hemofilters. UF rates were 1, 2, 3 and 6 L/hr with sufficient blood flow (Qb) to maintain UF rates (200–350 mL/min). Blood samples were collected from the pre-filter line and UF samples from the post-filter UF port. Concentrations of HP-CD in plasma and UF samples were assayed using qualified HPLC-fluorescence detection methods. Clearance was calculated using standard pharmacokinetic equations and differences in CI between the filter types were compared using a two-tailed, unpaired t-test. **Results:** See table. **Conclusion:** HP-CD is substantially cleared by CVVH. The HP-CD CI increases significantly with increasing UF rate but the CI did not differ by hemofilter type. HP-CD CI was independent of plasma concentration. CVVH CI at higher UF flows approximates the total CI reported in patients with normal renal function. CVVH may prevent HP-CD accumulation even in critically ill patients with acute renal failure.

Blood flow rates (Qb) (mL/min)	Clearance: AN69 Mean $\pm$ SD (n = 3) (mL/min)	Clearance: polysulfone Mean $\pm$ SD (n = 5) (mL/min)	p-value
Qb 200 mL/min, UF 1 L/hr	13.6 $\pm$ 2.84	12.7 $\pm$ 2.25	0.66
Qb 200 mL/min, UF 2 L/hr	30.9 $\pm$ 3.71	26.9 $\pm$ 5.99	0.28
Qb 300 mL/min, UF 3 L/hr	31.4 $\pm$ 15.7	38.7 $\pm$ 10.18	0.53
Qb 350 mL/min, UF 6 L/hr	103.2 $\pm$ 16.0	93.6 $\pm$ 8.48	0.41

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Trace Element Clearance in Critically Ill Patients Treated with Continuous Venovenous Hemodiafiltration (CVVHDF)

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Background: Nutrition support is an integral part of patient care in an ICU. Increasingly, critically ill patients with acute renal failure (ARF) are being treated with CVVHDF. Limited information is available on CVVHDF drug removal, far less is known about nutrient clearance during CVVHDF, particularly clearance of trace elements (TE). The aim of this study was to assess TE clearance in patients being treated with CVVHDF. **Methods:** TE (chromium,

copper, manganese, selenium, zinc) clearance was assessed in ten critically-ill adults (6 males, 4 females) treated with CVVHDF. Mean $\pm$ SD patient age was 47.7 $\pm$ 15.4 years and weight 80.2 $\pm$ 30.7 kg. Eight patients with ARF and two with ESRD were treated with CVVHDF for an average of 23.8 days (range 0.5–180). Nutrition support consisted of enteral feeding (n = 6) or parenteral nutrition (n = 2). The CVVHDF circuit used a polysulfone hemodiafilter (F-160NR, Fresenius n = 9, HF-1000, Gambro n = 1) with a dialysate flow rate of 2.05 $\pm$ 0.16 L/hr and ultrafiltration flow rate of 7.65 $\pm$ 3.0 mL/min. Samples were collected and stored using trace element-free materials. Samples were assayed for TE concentration using inductively coupled plasma mass spectrometry (ICP-MS). TE saturation coefficients were determined by obtaining a pre- and post-hemodiafilter blood samples and an effluent/spent dialysate sample. Average daily TE loss via CVVHDF was calculated and compared to typical daily TE supplementation in adult parenteral nutrition (MultitracTM-5 Concentrate, American Regent Laboratories, Inc.) **Results:** See table. **Conclusion:** Daily CVVHDF TE loss is minimal compared to the TE supplemented in daily parenteral nutrition and may result in TE accumulation. Considering tissue TE redistribution during stress and non-renal elimination routes for some TE, the clinical implications of our results and their possible effects on blood and tissue TE concentrations remain unknown. Adjustment of TE supplementation for CVVHDF patients may be necessary.

Trace element	Chromium	Copper	Manganese	Selenium	Zinc
Clearance mL/min ($\pm$ SD)	5.37 $\pm$ 2.25	0.455 $\pm$ 0.33	1.71 $\pm$ 3.96	1.58 $\pm$ 1.23	4.05 $\pm$ 1.37
Mean daily TE loss	4.21 mcg	0.011 mg	0.0002 mg	3.66 mcg	0.068 mg
Multitrac TM -5 concentration	10.0 mcg	1.0 mg	0.5 mg	60 mcg	5.0 mg
Supplied minus lost	5.79 mcg	0.989 mg	0.499 mg	56.34 mcg	4.93 mg

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The Use of APC during CRRT Obviates the Need of Additional Anticoagulation in Case of Septic Acute Renal Failure Using a Dose of 35 ml/kg/h

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Objectives: To determine or not if an additional anticoagulant is needed in case of use of APC during CRRT at 35 ml/kg/h for

Septic-Acute Renal Failure. **Background:** Despite recent publications of small case-series [1, 2], it has always been questioned whether or not additional anticoagulation is needed in case of APC therapy for Septic-Acute Renal Failure. Our study was aimed at bringing some additional pieces of information regarding this controversial and very practical issue. **Setting:** General Hospital, Regional Centre of 450 beds, Interland population of 150,000 inhabitants and a medical-surgical general ICU of 15 beds having 1000 admissions a year. The unit is performing from 40 CRRT patients up to 50 CRRT patients per year. **Design:** Prospective observational evaluation study and reported single centre experience. **Materials and Methods:** Ten consecutive ICU Septic-Acute Renal Failure Patients (they were eligible at the same time for CRRT at 35 ml/kg/h and eligible for Xigris) who were eligible for APC were enrolled in this prospective observational study with evaluation of mechanical filter life, need of additional anticoagulation, clotting testing. **Results:** There was no need of additional anticoagulation on top of APC in any of the 10 consecutive patients. The filter life was about 54 ± 6 hours which was greater than our usual filter life in the unit. The APTT was always above 60 sec in all our 10 patients during APC treatment. No significant bleeding did occur during APC treatment in these 10 cases. Also, we looked very carefully to the circuits, the filters and the venous chambers after cessation of the treatment and founded a significantly reduced clotting of these three parts of the extra-corporeal circuit. So, APC will probably also reduces aberrant clotting (Extra Body DIC) in the circuit, the filter and the venous chamber. So, not only the anticoagulant properties of APC will counted on this but also the reduction of 'Extra Body DIC'. **Conclusions:** During CRRT for Septic-Acute Renal Failure with Patients on APC, there is no need for additional anticoagulation on top of APC. The filter life appears to be well preserved. Mechanisms will include not only the anticoagulant properties of APC but also the reduction of 'Extra Body DIC'.

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Trace Mineral Clearance in Pediatric Patients Supported by Continuous Venovenous Hemodiafiltration (CVVHDF)

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Introduction: Pediatric intensive care patients increasingly being treated with CRRT like CVVHDF for fluid management, electrolyte imbalances, and sepsis. In all of these situations, provision of appropriate nutritional support is essential. A component of this nutrition is the administration of trace elements (TE). Limited information exists regarding TE clearance by any CRRT, and to our

knowledge no information on TE clearance has been published in pediatric patients. The purpose of this study was to assess TE clearance in pediatric patients requiring CVVHDF. **Methods:** Data was collected prospectively from five pediatric patients receiving CVVHDF for various indications during their ICU admission. The children were <18 years old and greater than 5 kg (dry weight). All five Prisma circuits used during the study were equipped with either the M60, AN-69 or the HF 1000 membranes, and operated in the CVVHDF mode. Blood flow ranged from 50–180 mL/min, dialysate rates from 19.2–38 mL/min/1.73 m², and effluent rates from 12.1–24 mL/min/1.73 m². Once consent was obtained, blood (arterial and venous), dialysate, and effluent samples were obtained from the dialysis circuit. The samples were then analyzed for zinc, copper, chromium, selenium, and manganese concentrations using inductively coupled plasma mass spectrometry (ICP-MS). TE saturation coefficients were calculated using pre- and post-hemodiafilter blood concentrations and effluent/spent dialysate concentrations. Average daily loss including total amounts, and per kilogram amounts, were calculated and compared to normal daily TE supplementation in pediatric parenteral nutrition (PTE-4) to determine net TE administration. **Results:** Five patients ranging from 10.5–53 kg and 23 months–15 years of age completed the study. Patient demographics were quite different, as were the indication for CRRT. Table-1 describes the percentage TE loss that is contributed to CVVHDF for each patient. **Conclusions:** (1) All TE were detected in the ultrafiltrate, however all were minimally cleared by CVVHDF. (2) Daily loss for all TE is far less than what is typically supplemented in parenteral solutions. (3) Upward adjustment of TE supplementation for CRRT loss unwarranted, and indeed, reduced TE supplementation regimens may be necessary.

Table 1.

Patient	Chromium (%)	Manganese (%)	Copper (%)	Zinc (%)	Selenium (%)
1	13.93	0.00	0.31	0.90	3.36
2	5.16	0.04	0.19	0.41	3.74
3	0.01	0.01	0.01	0.01	0.01
4	0.01	0.01	0.01	0.01	0.01
5	0.01	0.00	0.00	0.00	0.02

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Thyroid Hormone Transmembrane Clearance During Continuous Veno-venous Dialysis vs. Hemofiltration

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Introduction: This is a case report of a 16 -years-old female that presented in cardiac failure (EF < 3%) secondary to hyperthyroidism that required veno-arterial extracorporeal membrane oxygenation (ECMO) support and in-line CRRT for renal support. The patient

Table 1 for Abstract 51

Hormone (values)	Day 1 values pre-TPE	Day 2 values after one run TPE	Day 3 values after 2 runs TPE	Day 1 pre-TPE–Day 3 post 2 runs TPE	% decrease change day 1 vs. day 3	Day 1 TPE clearance (mL/min)	Day 2 TPE clearance (mL/min)
Total T3 (95–170 ng/dL)	181	104	75	106	58.56	30.48	32.45
Free T3 (2.8–5.3 pg/mL)	13.8	8.7	5.1	8.7	63.01	33.15	31.57
Total T4 (4.7–12.4 mcg/dL)	14.9	6.8	5.3	9.6	64.43	39.55	32.44
Free T4 (0.73–1.79 ng/dL)	4.65	4.65	2.83	3.62	56.12	31.56	30.57

weighed 69 kg (dry weight) and was 1.78 m². The indication for CRRT in this patient was anuric renal failure. There are a few literature reports of thyroid hormone clearance by CRRT. **Methods:** The patient was placed on CVVHD in-line with the ECMO circuit, using an Optiflux 160 (1.6 m²) hemodiafilter, blood flow of 210 mL/min, with a dialysate flow of 2000 mL/hour/1.73 m². During this time period samples of blood (arterial and venous) and effluent were obtained. After 30 minutes of hemodialysis the CRRT mode was switched to CVVH, the blood flow rate didn't change, and a new solution was hung for a pre-filter replacement fluid. The hemofiltration rate was also 2000 mL/hour/1.73 m². The saturation coefficient was calculated using the equation: $Sa = Ce / (Ca + Cv) / 2$, where Ce is the concentration in the effluent, Ca is the serum concentration of the patient pre-filter, and Cv is the serum concentration post-filter. Clearance was then calculated using the equation: $Cl = (Qd + Qe) \times Sa$. The sieving coefficient for the CVVH mode was calculated as $Sc = Ce / Ca$, where Ce is the concentration in the effluent, Ca already defined is the serum concentration of the patient pre-filter, pre-replacement fluid. Clearance was then calculated using the equation: $Cl = Sc \times \text{ultrafiltrate rate (UFR)}$. **Results:** The results are summarized in table 1. **Conclusions:** Thyroid hormones, free/bound T3/T4 are minimally removed by CVVHD and CVVH. CRRT did remove more free T3 compared to the other thyroid hormones; however this may or may not be clinically significant. CRRT should not be used for the indication of removing thyroid hormones for patients with significant hyperthyroidism.

Table 1.

Hormones (normals)	Sa CVVHD	Clearance CVVHD (mL/min)	Sc CVVH	Clearance CVVH (mL/min)
Total T3 (95–170 ng/dL)	0.16	5.26	0.17	5.67
Free T3 (2.8–5.3 pg/mL)	0.76	25.26	0.71	23.68
Total T4 (4.7–12.4 mcg/dL)	0.02	0.68	0.02	0.65
Free T4 (0.73–1.79 ng/mL)	0.11	3.51	0.10	3.39

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Thyroid Hormone Transmembrane Clearance During Therapeutic Plasma Exchange

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Introduction: A rare life-threatening complication of hyperthyroidism is thyroid storm. The goal of treatment is to reduce the production and/or secretion of thyroid hormone production by the thyroid gland thus reducing the circulating levels of free T4 and T3. We present a case of a 16 year-old girl who presented in cardiogenic shock secondary to hyperthyroid storm who required veno-arterial extracorporeal life support (ELS). Her initial therapy of propylthiouracil, potassium iodide and hydrocortisone failed to reduce her thyroid hormone levels. Continuous veno-venous hemodialysis (CVVHD) was initiated, followed by therapeutic plasma exchange (TPE) in the attempts to remove the thyroid hormones. **Methods:** The patient was placed on TPE using a Prisma circuit, TPE 2000 plasma exchange filter at a blood flow rate of 180 mL/min and a replacement rate of 750 mL/hr initially, and then was increased to 2000 mL/hr for 3 hours. TPE was done for two consecutive days. During this time period samples of blood (arterial and venous) and effluent were obtained immediately after TPE was initiated and then at the end of the run. The TPE coefficient was calculated using the equation: $STPE = Ce / (Ca + Cv) / 2$, where Ce is the concentration in the effluent, Ca is the serum concentration of the patient pre-filter, and Cv is the serum concentration post-filter. Clearance was then calculated using the equation: $ClTPE = (Qd + Qe) \times STPE$. The patient was replaced with a total of 5500 mL of a 50% combination of fresh frozen plasma (FFP) and 5% albumin post hemodiafilter. **Results:** The results of this report are summarized in table 1. **Conclusion:** TPE seems to enhance bound and free T3 and T4 removal, and most likely removes other molecules of small and large molecular weights with varying degrees of protein binding. Further clinical studies are needed to determine the clinical possibilities of this treatment. However, based on our case study TPE is a treatment option for treatment of acute thyroid storm.

Fluid Removal Rate and Mortality in Pediatric CRRT: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group

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Previous work has demonstrated that pediatric patients undergoing CRRT who have higher levels of fluid overload at initiation of therapy have an increased risk of mortality. No studies to date have examined the relationship between fluid removal rates and mortality in pediatric CRRT patients. We conducted a retrospective cohort

study of 188 patients from 13 US centers using a multivariable logistic regression model to test the hypothesis that higher rates of fluid removal from volume overloaded patients are associated with reduced mortality. Volume status was measured for each subject from the time of ICU admission to CRRT initiation; fluid excess was defined as the difference between total fluid intake and output. Subjects were then divided into cohorts based on the percentage of excess fluid removed in the first 72 hours of therapy: those who had 0 to 50% excess fluid removed ($n = 60$), 50% or more excess fluid removed ($n = 56$), and those in whom no fluid was removed ($n = 72$). The model included the following covariates: GFR at CRRT initiation, age, gender, PRISM II score, % fluid overload at CRRT initiation, and number of vasopressors used. Patients who had <50% of their fluid excess removed by 72 hours had an adjusted odds ratio for mortality of 3.2 (95% CI 1.2 – 8.2, $p = 0.018$) compared with patients who had 50% or more of their excess fluid removed. We conclude that less fluid removal in the first 72 hours of therapy is associated with a greater risk of mortality when controlling for severity of illness. Prospective trials are needed to determine the appropriate fluid removal rates in fluid overloaded pediatric CRRT patients.

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