

# CRRT 2013

## EIGHTEENTH INTERNATIONAL CONFERENCE ON CONTINUOUS RENAL REPLACEMENT THERAPIES

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CRRT 2013

#### Epidemiology and Outcomes from AKI

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# EPIDEMIOLOGY AND OUTCOMES FROM AKI

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## 1. Risk Factors and Clinical Courses of Acute Kidney Injury in Patients with Femur Fracture

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**Purpose :** Femur fracture is mostly occurred in elderly patients and highly associated with medical problems such as acute kidney injury(AKI), but there are few reports about AKI in femur fracture patients. So this study was performed to figure out risk factors and clinical courses of AKI in patients with femur fracture by falling.

**Methods :** We retrospectively evaluated the medical records of 110 patients with femur fracture between November 2006 and December 2011 in Uijeongbu St. Mary's hospital. We investigated the incidence and clinical courses of AKI in femur fracture patients, and we compared the clinical findings between AKI and normal kidney function(NKF) groups.

**Results :** Of the total 110 femur fracture patients, AKI was observed in 19 patients(17.3%). The peak serum creatinine level in AKI patients was  $2.59 \pm 1.57$  mg/dL. 2 of 19 AKI patients died and 2 patients progressed to chronic kidney disease. When compared to NKF group, the AKI group had higher incidence of elevated LDH (63.2% vs 34.1%,  $p=0.020$ ), ESR (31.6% vs 6.6%,  $p=0.008$ ), and CRP (57.9% vs 46.2%,  $p=0.042$ ). The AKI group also had longer time duration between injury and operation, and post-operation hospital day, and more prescribed ACE inhibitor than NKF group. Multivariate analysis demonstrated elevated LDH, ESR and ACE inhibitor prescription as independent risk factors of AKI in femur fracture.

**Conclusion :** The incidence of AKI in femur fracture patient was 17.3% and AKI were associated with longer clinical course. Close observation of clinical and laboratory findings are recommended in patients with femur fracture and early management should be performed for reducing the morbidity of AKI patients.

	Regression Coefficient	p-value	Adjusted Odds Ratio	95% C.I.
Sex	2.004	0.167	7.417	0.433 - 127.147
Diabetes	1.597	0.267	4.940	0.294 - 82.889
Increased LDH	3.319	0.040	27.644	1.156 - 660.807
Increased ESR	2.259	0.035	9.574	1.176 - 77.957
ACE inhibitor	5.292	0.013	198.646	2.986 - 13216.654

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## 2. Acute Kidney Injury Outcomes in Chronic Kidney Disease Patients with Clostridium difficile Infection

Mira T Keddiss<sup>1</sup>, Sahil Khanna<sup>1</sup>, Larry M Baddour<sup>1</sup>, Darrell S Pardi<sup>1</sup>, Qi Qian<sup>1</sup>

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**Introduction:** To assess acute kidney injury (AKI) outcomes in a national cohort of hospitalized chronic kidney disease (CKD) patients with clostridium difficile infection (CDI).

**Methods:** We analyzed national hospital discharge survey (NHDS) database from 2005-2009 and collected information on demographics, ICD-9 diagnosis, procedure codes, discharge information and in-hospital mortality. Clinical information was

abstracted and analyzed using SAS version 9.2 and JMP version 9.0.1.

**Results:** Of the 8.03 million CKD patients, an estimated 119,421 (1.49%) had a diagnosis of CDI. A diagnosis of AKI was

present in 1.55 million (19.4%) of all patients with CKD and was most common among patients with unspecified CKD diagnosis (49.3%). A total of 2.21 million (27.5%) required renal replacement therapy during their hospitalization, of whom 93.2% were patients with CKD V on chronic dialysis. Seven percent of patients with AKI required renal replacement therapy. Characteristics and outcomes of AKI in CKD patients with CDI diagnosis are shown in Table 1. Conclusion: CKD patients who develop AKI in the setting of CDI are at significantly higher risk of adverse morbidity and mortality during their hospitalization.

Characteristics	AKI	No-AKI	P value	Adjusted OR, P value
Age (median,range)	76 (21, 93)	74 (25, 97)	0.0405	-
Gender (% male)	55.4%	54.2%	0.0004	-
Race (%Caucasian)	75.1%	76.6%	<0.0001	-
Length of stay, days (median, range)	10 (1, 60)	7 (1, 68)	0.0033	-0.986, 0.0084
Dismissal to care facility	48.2%	43.2%	<0.0001	1.11, <0.0001
Colectomy	1.58%	0.36%	<0.0001	2.17, <0.0001
Mortality	10.8%	5.23%	<0.0001	2.18, <0.0001

### 3. The Association between Social Support and Psychosocial Factors upon Mortality and Quality of Life

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#### Background:

Treating End Stage Renal Disease (ESRD) by hemodialysis (HD) creates changes to relationship patterns, social life, activities of daily living and the ability to attain a satisfactory Quality of Life (QoL). There is an absence of information in Saudi Arabia on the impact of these changes in the renal population.

#### Objective

This study investigated the influence of social support and other psychosocial factors upon mortality, adherence to medical care recommendations, and physical QoL amongst hemodialysis patients.

#### Method

272 HD patients were examined using the QoL questionnaire to determine self-reported inclinations. Logistics regression through Weighted K was used to analyze data.

#### Results

53.5% of patients reported health had interfered with their social activities demonstrating a strong associated with risk towards All-Cause (sp=1.33) and Cause-Specific Mortality including cardiac diseases (sp=1.28). These patients had a greater risk of withdrawing (sp=1.67) from treatment, non- adherence to Phosphorus (sp=1.06) greater than 7.5 mg/dL and increased risk towards an albumin of less than 3.5 g/dL (sp=1.23). Patients reporting dissatisfied with family support (12.0%) were at highest risk to non-adherence to intra-dialytic weight gain (sp=1.27), shortening the dialysis session (sp=1.21) and increased risk of Potassium level greater than 6 mEq/L (sp=1.14). However, patients reporting dissatisfied with staff support (14.1%) revealed a higher risk of decreased physical QoL (sp=0.76).

#### Conclusion & Application to Practice

This study demonstrated that physical QoL was not only affected by medications and other laboratory work-ups but also with additional psychosocial support. The study led to the development of programs empowering patients and families to participate in their treatment plans. The program includes various counselling approaches directed to patient, families, and health team.

#### 4. The value of B-type natriuretic peptide for prognosis of critically ill patients requiring CRRT

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**Purpose:** AKI in the ICU is a serious complication that can affect the patient outcome. B-type natriuretic peptide (BNP) level which measured at ICU admission is useful in evaluating heart failure, but its role in evaluating patients with AKI requiring CRRT is unclear. The aim of this study was to evaluate role of BNP and prognostic factors in ICU patients with AKI requiring CRRT

**Method:** We retrospectively reviewed the medical records of all ICU patients who received CRRT at Dong-A university hospital from March 2011 to September 2012. The prognostic values of BNP for the mortality during CRRT were investigated, and their cutoff values for death were determined.

**Results:** The total number of patients who required CRRT in ICU was 89. The average age of the 89 patients was  $54.0 \pm 18.4$  years and 45 patients were male (51.0%). The treatment duration of CRRT was  $72 \pm 34.6$  hours. The mean BNP levels of the 25 patients who died were significantly higher than that of those who survived (2280 versus 850pg/mL;  $P < 0.05$ ). The area under the curve was 0.93 and optimal threshold for BNP was 1429pg/mL. Patients with BNP levels more than the threshold of 1389pg/mL is the independent factor predicting mortality during CRRT (odds ratio 39.6; 95 CI, 5.79-271).

**Conclusions:** Among critically ill patients, BNP level more than 1429pg/mL is an independent marker of mortality in patients during CRRT. A large scaled, prospective randomized multi-center trials are needed to confirm the validation of the optimal threshold and independent predictive power of BNP in the critical care setting.

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#### 5. Nephrotoxic Medication Associated Acute Kidney Injury leads to Chronic Kidney Disease Development at 6 Months

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**Background/objective:** Nephrotoxic-medication exposure is a common cause of Acute Kidney Injury (NTMx-AKI) in hospitalized children. No longitudinal data exist to assess for post-hospitalization kidney outcomes after such an episode. We aimed to assess the medium-term outcome after NTMx-AKI.

**Design:** We did a retrospective outcome assessment for non-critically ill children (pt) exposed to an IV aminoglycoside for >3 days or >3 NTMx simultaneously who developed AKI by the pRIFLE criteria from June 2011 to May 2012. All had daily serum creatinine (SCr) monitored during hospitalization as part of institutional practice. Follow-up data > 6 months after AKI were retrieved from medical records.

**Results:** 100 pt (mean age  $9.30 \pm 6.9$  yrs) with NTMx-AKI were identified. The primary services involved were Bone Marrow Transplant/Oncology (59%), Liver Transplant (13%), Pulmonary (13%), and Surgery (5%). Mean pre-AKI eGFR was  $118.8 \pm 14.9$  mL/min/1.73m<sup>2</sup> and was between 90-150 mL/min/1.73m<sup>2</sup> for all. 0/15 pt assessed had urine protein to creatinine ratio (Up:c) >0.2. Maximum pRIFLE strata was 'R' in 23 pt (23%), 'I' in 63 (63%) and 'F' in 14. Mean AKI duration was  $11.4 \pm 9.8$  days. 4 pt received renal replacement therapy. 92 pt survived to discharge. Mean eGFR at discharge was  $105.1 \pm 27.2$  mL/min/1.73m<sup>2</sup>; 22 (23.9%) had eGFR <90 and 5 < 60 mL/min/1.73m<sup>2</sup>.

At 6 months post-NTMx-AKI, data were available for 80 pt (6 had no follow up, 6 deceased). 77/80 had a follow up SCr; Mean eGFR was  $113.3 \pm 30.6$  mL/min/1.73m<sup>2</sup>. 18 (22.5%) pt had eGFR <90, 2 <60 and 9 (11.2%) had eGFR >150 mL/min/1.73m<sup>2</sup>. Mean Cystatin C GFR was  $80.2 \pm 23.4$  mL/min/1.73m<sup>2</sup> (n=52). 27/34 assessed pt had Up:c >0.2. 29 pt had hypertension. Only 15 (17.2%) were seen in a pediatric nephrology clinic; 11 of whom showed 1+ sign of Chronic Kidney Disease (CKD) (proteinuria, hypertension or impaired eGFR). Overall, 58 pt (72.5%) had at least 1 sign of CKD; 18 had 2 signs, 4 pt had 3; however only 34 (42.5%) had a complete evaluation of blood pressure, serum creatinine and proteinuria.

**Conclusions:** 6 months after NTMx-AKI, residual kidney damage in the form of reduced GFR, hyperfiltration, proteinuria or



hypertension is seen in a large number of non-critically ill children. However less than 50% undergo a complete evaluation for CKD and only 20% are seen by a nephrologist. With studies showing an association between AKI and CKD, we suggest systematic comprehensive follow up is essential to assess for CKD in children after NTMx-AKI.

## 6. Acute Kidney Injury in Pediatric Hematopoietic Stem Cell Transplant Patients Predicts Day 100 Mortality

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**Background:** Acute kidney injury (AKI) has been previously shown to be an independent predictor of poor outcomes in many patient populations. Previous studies have shown that even mild AKI is associated with chronic kidney disease and mortality in patients undergoing Hematopoietic Stem Cell Transplant (HSCT).

**Objective:** Determine the incidence of AKI in pediatric patients during the first 7 and 30 days following HSCT, and to examine the association between the presence of AKI and 100 day, 1 year survival.

**Design/Methods:** We retrospectively reviewed data on 132 consecutive pediatric patients who received HSCT at The Children's of Alabama Hospital between 2000-2007. AKI was defined using modified AKIN criteria Baseline SCr values for all patients were obtained during the pre-transplant evaluation. The incidence of AKI was determined at 7 and 30 days post-transplant.

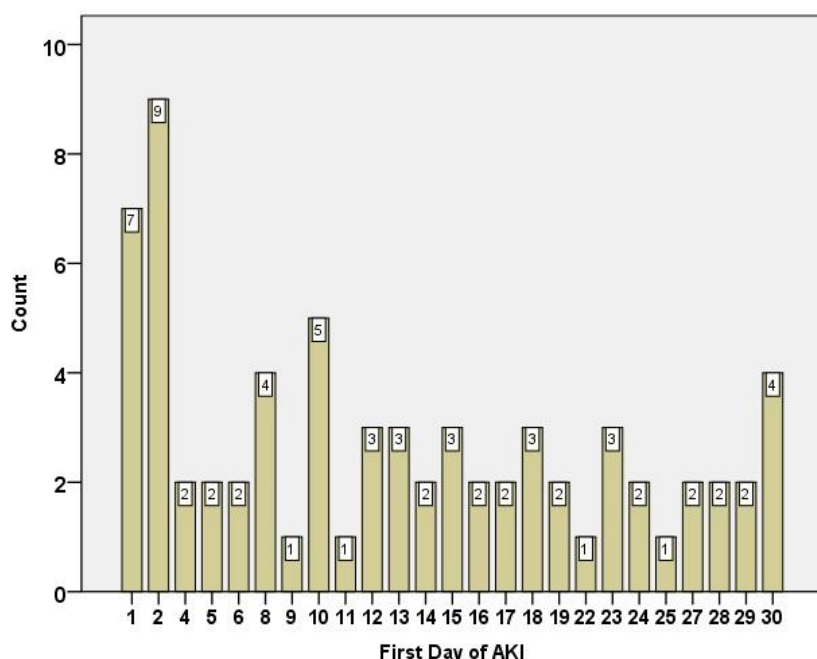
**Results:** 23/ 132 (17%) patients met the AKI criteria during the first week post-HSCT and 70 of 132 (53%) of patients met criteria for AKI During the first 30 days following HSCT. As opposed to incident of AKI in NICU population in which 82% of AKI occurs in first week of admission, incident AKI occurred throughout first 30 day post HSCT.

**Conclusions:** This study shown that later development of AKI (by day 30) is associated with increased day 100 mortality. Future studies are planned to determine potential interventions to prevent or treat AKI, which could improve outcomes for this at-risk population.

(figure on following page)

	AKi 7 Days	Aki 30 days
No AKI	109/132 (82%)	62/132 (47%)
AKI 1	8/132 (6%)	19/132 (14%)
AKI 2	9/132 (7%)	30/132 (23%)
AKI 3	6/132 (5%)	21/132 (16%)
100 Day Mortality	3/19 (16%)	14/19 (73%) (p=0.05)
1 Yr Mortality	4/43 (9%)	25/43 (58%) (p=0.4)





## 7. Acute Kidney Injury Following Pulmonary Thromboendarterectomy

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Purpose of the study: Pulmonary thromboendarterectomy (PTE) is an established technique to improve pulmonary and cardiovascular function in chronic thromboembolic pulmonary hypertension (CTEPH), however its effect on renal function is not known. Since PTE surgery requires complete circulatory arrest, we hypothesized that it would be associated with development of acute kidney injury (AKI). In addition, we postulated that the enhancement in cardiovascular performance would result in an improvement in renal function at hospital discharge.

Methods: We reviewed data from 123 adult patients with CTEPH undergoing PTE enrolled in a prospective trial of a lung protective ventilation strategy to prevent acute lung injury. AKI was determined by the AKIN/KDIGO AKI serum creatinine and urine output criteria. Outcomes included duration of mechanical ventilation, intensive care unit and hospital stay, and renal function at discharge.

Summary of the results: Fifty-one (41%) patients developed AKI following PTE surgery; 25 (20%) met the serum creatinine and 26 (21%) the urine output criteria. Underlying chronic kidney disease (estimated GFR < 60 ml/min per 1.73 m<sup>2</sup>) was present in 10% and was more frequent in patients with acute kidney injury. The mean time to development and duration of AKI were 2.7 and 2.3 days, respectively. AKI and no-AKI patients had a similar duration of ventilator requirement (median of 1.0 day, p=0.77) and significantly longer median lengths of stay in the ICU and hospital. At discharge, renal function had improved in 40.6%, was unchanged in 56.1%, and had worsened in 3.3%. A similar trend was seen in patients with pre-existing chronic kidney disease (n=13) with over 76% showing improvement to an estimated GFR >60 ml/min.

Conclusion: We observed a high incidence of AKI following PTE which was associated with worse outcomes. Renal function improved following PTE and was similar in AKI and no-AKI patients. These findings highlight the importance of measuring renal function changes in CTEPH patients undergoing PTE.

## 8. Five-year Risk of End-stage Renal Disease after Surviving Dialysis-requiring Acute Kidney Injury among Intensive Care Patients: A Nationwide Cohort Study

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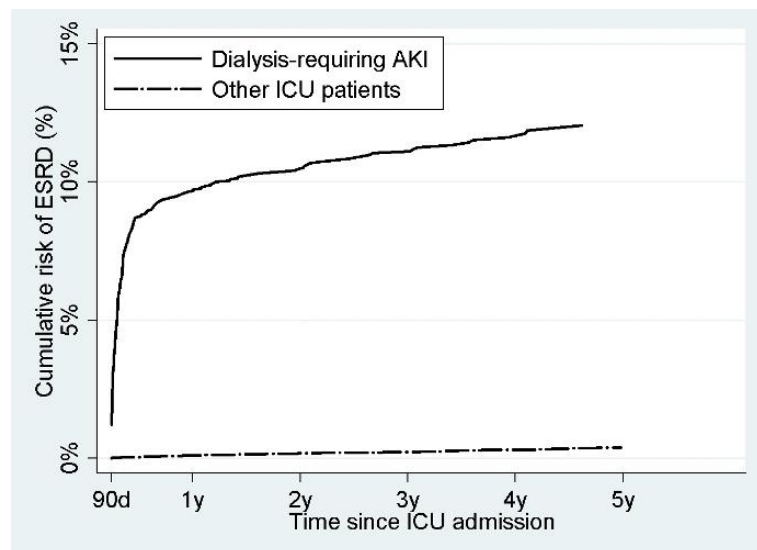
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**Purpose:** Dialysis-requiring acute kidney injury (AKI) is common among intensive care unit (ICU) patients. However, follow-up data on risk of end-stage renal disease (ESRD) among these patients remain sparse. Among patients surviving 90-days after ICU admission, we assessed the 5-year risk of ESRD after dialysis-requiring AKI and compared it with the risk in other ICU patients. We also assessed the risk within subgroups of ICU patients.

**Methods:** We used population-based medical registries to identify all adult patients admitted to an ICU in Denmark (population 5.5 mill.) from 2005 through 2009, who survived 90 days after ICU admission. We computed cumulative ESRD risk, accounting for death as a competing risk, for patients with dialysis-requiring AKI and for other ICU patients. We estimated hazard ratios (HR) as a measure of relative risks using a Cox regression model adjusted for potential confounders. Dialysis-requiring AKI was defined as need for acute dialysis upon or after ICU admission, as coded in the Danish National Registry of Patients. The reference cohort was ICU patients' not receiving acute dialysis ('other ICU patients'). ESRD was defined as chronic need of dialysis or kidney transplant. We repeated the analyses within subgroups of ICU patients.

**Results:** We identified 91,615 patients who survived to 90 days after ICU admission. Of these, 2521 (2.8%) had an episode of dialysis-requiring AKI. The overall 5-year ESRD risk was 12.7% (95% confidence interval [CI] 11.4–14.0) for ICU patients with an episode of dialysis-requiring AKI, compared with 0.4% (95% CI 0.3–0.5) for other ICU patients (fig). Within the 90-day to 180-day time period the ESRD risk for dialysis-requiring AKI patients was 8.7%, compared with 0.1% for other ICU patients. This corresponded to an adjusted HR of 121.5 (95% CI 87.6–168.6). Among patients who survived 180 days after ICU admission without developing ESRD (n=86,205), the 181-day to 5-year ESRD risk was 4.0% for patients with dialysis-requiring AKI, compared with 0.4% for other ICU patients, corresponding to an adjusted HR of 6.7 (95% CI 5.0–9.1). The relative impact of dialysis-requiring AKI was evident within all subgroups of ICU patients. However, the impact was most pronounced among patients without a preexisting diagnosis of chronic kidney disease and in elective surgical patients.

**Conclusion:** Dialysis-requiring AKI is an important risk factor for ESRD up to five years after ICU admission.



## 9. Retrospective Monocentric 10-Year Analysis Of Sepsis-Associated Acute Kidney Injury: Impact On Outcome, Dialysis Dose And Residual Renal Function

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Introduction and aim of the studies: Sepsis is the predominant causes of acute kidney injury (AKI) in critically ill patients. Septic AKI is associated with multiple organ failures and high mortality rates. The aims of this study were to evaluate the incidence of sepsis as cause of AKI and to identify its impact on the management of dialysis and on outcome.

Methods: We analyzed all patients admitted to ICU treated by renal replacement therapies (RRT) for AKI in the period 2001-2010. RIFLE, SOFA and ATN\_ISS scores were calculated. Diagnosis of sepsis/septic shock was performed according to published criteria. Patients' outcome and renal function were evaluated 28 days after ICU admission. Statistical analysis was performed using the Hemer-Lemeshow test.

Results: We treated by RRT 1833 patients with AKI (9061 sessions performed). Patients characteristics were: 64.7% males; age 66.4±11.5 yrs; serum creatinine at the start of RRT 3.8±1.9 mg/dl; RIFLE Failure 56.8%, Injury 28.4%, Risk 14.8%; SOFA 10.6±1.3; number of organ failures: 3.4±1.3; ATN\_ISS 0.738±0.192. At day 28, mortality was 1257/1833 (68.6%). The observed mortality was significantly lower than that expected by the ATN\_ISS score (72%), (p<0.05). Sepsis was the main cause of AKI: 415/1833 (22.6%). We distinguished 2 groups: the septic group (S) and the non-septic group (NS, 1418/1833: 77.4%). In the S group, mortality at day 28 was 302/415 (72.9%), whereas in NS group was 804/1418 (56.7%), (p<0.05). The expected mortality in the S group was 73.8%, whereas in the NS group was 72%. In the surviving patients, serum creatinine at day 28 was 2.69±0.72 mg/dl in the S group and 2.12±0.62 mg/dl in the NS group (p>0.05). In a small cohort of patients (n=50), administered dose was significantly higher in the S group (36.84±8.42 ml/Kg/h) than in the NS group (25.93±5.16 ml/Kg/h).

Conclusions: Our retrospective analysis showed that: 1) sepsis was the most relevant cause of AKI; 2) mortality in the S group was significantly higher than in the NS group; 3) only in the NS group the observed mortality was lower than the expected; 4) AKI leads to a possible progression toward chronic kidney disease in both groups; 5) administered dose in the S group was higher than in NS group, suggesting that S group is subjected to a more intense dialytic treatment with the aim to limit fluid overload and to remove circulating inflammatory mediators.

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## 10. Impact of Early Fluid Overload on Mortality in Critically Ill Children

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Background: Fluid overload (FO) is a common problem in critically ill children and has been associated with adverse outcomes. Our objective in this retrospective cohort study was to assess the impact of early FO on mortality in children admitted to the intensive care unit (ICU) with sepsis and/or shock states. Methods: We performed a retrospective chart review of critically ill children in a tertiary level pediatric ICU, admitted between September 1, 2009 and March 31, 2010 with sepsis and/or shock as one of the admitting diagnoses. Children with an ICU stay < 2 days and were excluded. FO was defined as fluid accumulation > 10% admission body weight of the patient. Cumulative fluid accumulation was measured daily for up to 7 days after ICU admission. Survivors and non-survivors were compared with respect to early FO factors including maximum fluid accumulation, presence of FO during initial 3 days and number of days with FO during the initial 7 days. Multivariable logistic regression analysis was performed to identify independent predictors of mortality. Results: A total of 116 patients met criteria and were included in the study. Age ranged from 0 to 17.4 years with a median of 1.1 years. Maximum cumulative fluid accumulations in the initial 3 days as well as in the initial 7 days of ICU stay were significantly higher among non-survivors, with a 3-day median of 5% vs. 13.5% and 7-day median of 7% vs. 18.5% for survivors and non-survivors respectively (p-value < 0.001) (Figure 1). Severity of illness at admission (Paediatric Index of Mortality 2), need

for vasopressor support and renal dysfunction were significantly higher as well among non-survivors. There was no significant difference with respect to age, gender, hospital days prior to ICU admission, primary diagnoses, reason for ICU admission, presence of oncologic diagnosis and presence of respiratory failure at admission. Multivariable logistic regression analysis identified maximum cumulative fluid accumulation during initial 3 days (Adjusted OR 1.56, p-value 0.003) as well as 7 days (Adjusted odds ratio 1.21, p-value < 0.001), presence of early FO (initial 3 days) (Adjusted odds ratio 8.20, p-value 0.004) and number of days of FO during the initial 7 days (Adjusted odds ratio 3.43, p-value 0.001) as independent predictors of death. Conclusion: In our cohort of critically ill children with sepsis and/or shock states, early FO, severity of FO and duration of FO have significant impact on mortality.

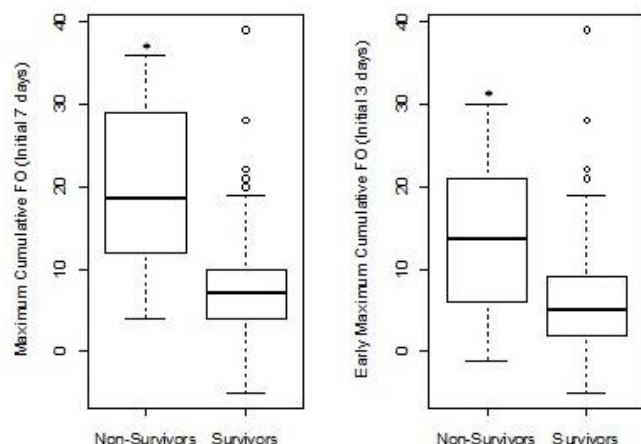


Figure 1: Maximum cumulative fluid overload – Non-survivors Vs. Survivors (\* p-value < 0.001)

## 11. AKI severity not duration affects long term mortality in critically ill patients

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**Background :** Acute kidney injury (AKI) is a common clinical problem in hospitalized patients, especially in those who are critically ill. AKI has 3 factors such as severity, duration and reversibility. Severity effect has confirmed various studies. However, it is not known how adverse long term outcome vary according the duration of AKI. This study was performed to determine whether duration and severity of AKI are associated with long term mortality in critically ill patients.

**Methods :** We prospectively enrolled 274 patients who admitted to intensive care units in tertiary hospital center for 1 year . Duration of AKI was defined by number of days AKI was present and categorized as no AKI , AKI for 1 to2, 3 to 6, at least 7 days and persistent AKI. And the severity of AKI was classified by AKIN staging criteria. Kaplan-Meier curves were used to determine the 4 year survival rate. Mortality was adjusted according to the Cox proportional hazards model.

**Results :** Among ICU patients 29.6% of patients exhibited AKI in ICU patients during the study period. Among these patients, 39(14.2%) had stage 1, 8(2.9%) stage 2; and 34(12.4%), stage 3 disease. The proportion of patients with AKI duration were as follow : 1 to 2 days (23; 8.4%), 3 to 6 days (11; 4.0%), at least 7 days (7; 2.6%), persistent AKI (40; 14.7%). Four year mortality for patient with 1 to 2 days duration group was significantly higher than that for patients with no-AKI group (91.7% vs 54.5%, p<0.000). But, mortality was not significantly differently by AKI duration except persistent AKI. The Cox analysis showed the patients with AKI stage 3 were associated with mortality (hazard ratio, 11.0; 95% confidence interval, 4.7 to 25.0, p<0.001).

**Conclusions :** Long term outcome depended on AKI severity. However duration of AKI did not affect AKI mortality. Our findings suggest that physicians should pay attention to patients who suffered from AKI even after they fully recover.

## 12. The Impact Of Early Postoperative Acute Kidney Injury On One-Year Risk Of Myocardial Infarction, Stroke And Death Among Patients Undergoing Elective Cardiothoracic Surgery: A Cohort Study

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### Objectives:

Studies on the long-term prognostic impact of acute kidney injury (AKI) after elective cardiothoracic surgery remain sparse. We therefore examined the one-year risk of acute myocardial infarction (AMI), stroke and death after elective cardiothoracic surgery complicated by AKI.

### Methods:

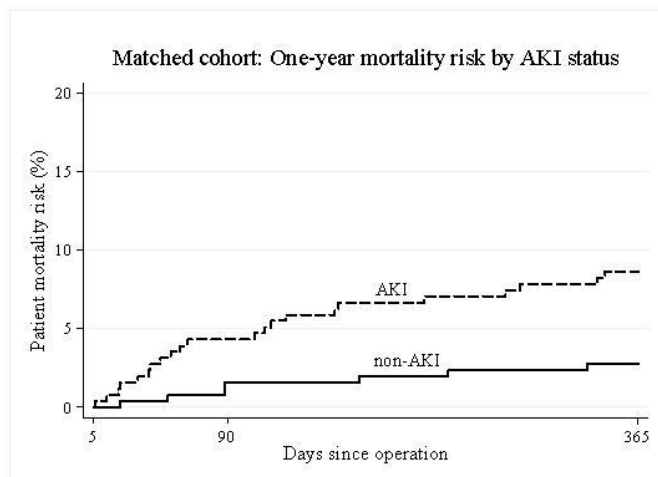
We conducted a cohort study among 1,030 adult elective cardiothoracic surgical patients from the Department of Cardiothoracic and Vascular Surgery, Aarhus University Hospital, Denmark. Patients were included between April 1, 2005 and October 8, 2007. Exclusion criteria were severe kidney disease (s-creatinine >2.3mg/dL (200μmol/L)) and previous heart or renal transplant surgery. AKI was defined as more than 50% increase of s-creatinine from baseline level, acute rise (within 48 hours) of 0.3mg/dL (26.5μmol/L) or more, and/or initiation of renal replacement therapy within the first four days after surgery. There were complete baseline s-creatinine measurements for the study population. Follow-up began on the fifth post-operative day. Outcome data on AMI, stroke and death within a year after surgery were obtained through linkage to the Danish National Registry of Patients and the Danish Civil Registration System. Using propensity score analyses, we matched 255 AKI patients with 255 non-AKI patients. In this matched cohort we computed the cumulative risk of AMI, stroke and death using a cumulative incidence method and the corresponding hazard ratios for each outcome by Cox regression.

### Results:

A total of 287 (27.9%) of the 1,030 patients experienced an episode of AKI. AKI patients were older, had higher level of comorbidity and higher baseline s-creatinine values. Covariates were adequately balanced after propensity score matching. In the matched cohort one-year cumulative risk of AMI was 2.0% (95% CI: 0.7–4.3) for AKI patients and 1.2% (95% CI: 0.3–3.2) for non-AKI patients. One-year cumulative risk of stroke was similar in the two exposure groups; 1.6% (95% CI: 0.5–3.7). HRs for AMI and stroke was 1.7 (95% CI: 0.4–7.1) and 1.0 (95% CI: 0.3–4.1), respectively. One-year cumulative mortality risk was 8.6% (95% CI: 5.8–12.8) among patients with AKI compared to 2.8% (95% CI: 1.3–5.7) for patients without AKI. This corresponds to a HR of 3.2 (95% CI: 1.4–7.6).

### Conclusion:

AKI was associated with increased mortality up to one year after elective cardiothoracic surgery. The risk of AMI was insignificantly increased, whereas no association was found for stroke.



### 13. Incidence and Clinical Course of Acute Kidney Injury in Adult Patients with Severe Trauma

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<sup>1</sup>The Catholic University of Korea Medical College, <sup>2</sup>Inje University Medical College

**Purpose:** Severe trauma is a traumatic injury to cause single or multiple lesions that are immediately or potentially life threatening. Although acute kidney injury (AKI) is thought to commonly develop in patients with severe trauma, it is rarely reported. This study was performed to the incidence and clinical course of AKI in adult patients with severe trauma.

**Methods:** We retrospectively evaluated the medical records of 150 adult patients with severe trauma between January 2011 and December 2011 in a single University Hospitals. We investigated the incidence and clinical course of AKI, and mortality in severe trauma patients. Severe trauma was defined as more than 15 of injury severity score.

**Results:** Mean age of the patients was 50±17 years (18-94 years) and the number of male was 110. Of the total 150 patients, the number of diabetes mellitus, hypertension, were 11 (7.3%), 16 (16.1%), but chronic kidney disease was never seen. The incidence of hypotensive shock at admission was 14.0% (n=21) and 19 patients (12.7%) died during admission. AKI was observed in 30 patients (20%). The peak serum creatinine level in AKI patients was 3.38±1.75 mg/dL (1.53-7.89 mg/dL). AKI developed within 3 days after admission in 27 of 30 patients. Of the total 30 AKI patients, 6 patients (20%) received CRRT. Thirteen patients (43.3%) survived with complete improvement of kidney function and 17 patients died without kidney improvement. When compared to normal renal function group (n=120), AKI group (n=30) had higher mortality (56.7% vs 1.3%, p<0.0001).

**Conclusion:** The incidence of AKI was high (20%) in patients with severe trauma and AKI patients showed higher mortality, compared to patients with normal renal function.

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### 14. Microbiology and Clinical Outcomes of Sepsis in Acute Kidney Injury Patients

Soo Young Yoon<sup>1</sup>, Jae Hyuk Lee<sup>1</sup>, Kyung Won Park<sup>1</sup>, Kkot Sil Lee<sup>1</sup>, Sung Jin Moon<sup>1</sup>

<sup>1</sup>Kwandong University College of Medicine

**Purpose:** Acute kidney injury (AKI) patients treated with continuous renal replacement therapy (CRRT) are associated with increased mortality. Sepsis-related multi-organ dysfunction is a major cause of death in this population. To evaluate the etiology and the effect on mortality of sepsis in AKI patients, we conducted a retrospective observational study using medical records of AKI patients treated with CRRT in 20-bed ICU over 8-year period.

**Methods:** Among 334 patients treated with CRRT, after excluding 101 previously dialyzed patients and 42 paraquat-poisoning patients, 191 AKI patients were identified. We evaluated the microbiology and origin of sepsis. To define the effect of sepsis on in-hospital mortality, we stratified the patients into 3 groups according to their blood culture results; no culture performed, culture positive, and culture negative.

**Results:** Of the 191 patients, 119 (62.3%) were male and mean age was 69.4 years. More than 50% of the patients admitted due to cardiac (25.1%) or renal (30.4%) problems and 12.6% experienced surgery. Blood culture was performed in 169 patients (88.5%) and among them, 67 patients (39.6%) showed positive results. Among 67 septic patients, 29 (43.3%) failed to reveal their infectious origin, otherwise, 21 (31.3%) had UTI and 11 (16.4%) had pneumonia. Duration on CRRT was longer in blood culture negative group but ICU or hospital lengths of stay were not different among three groups. Blood culture positive group had more patients with acute lung injury and multi-organ dysfunction than other two groups. ICU and hospital mortalities were higher in blood culture positive group than negative group, but they were similar between the patients with blood culture positive and the patients did not perform blood culture. When we compared the microbiology



between the period 2004-2007 and 2008-2012, there were more patients with negative blood culture results in year 2008-2012 than those in year 2004-2007 (62.8% vs. 39.7%, respectively) among blood culture drawn patients. While predominant organisms were *S. aureus* and *S. epidermidis* in 2004-2007, *A. baumannii*, *E. coli*, and staphylococcus other than aureus and epidermidis were identified frequently in 2008-2012.

Conclusion: This study shows exclusive data describing microbiology and consequences of sepsis in AKI patients in ICU. In addition, we recognized that organisms identified in blood stream were changing as times go by.

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## 15. Acute metabolic acidosis with low or positive anion gap in the setting of salicylate intoxication

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<sup>1</sup>Mayo Clinic - Rochester

Acute metabolic acidosis associated with a reduced anion gap (AG) or a positive AG is rare. There have been several case reports of such abnormality occurring in the setting of acute salicylate intoxication. The underlying etiology of this phenomenon is unclear.

We reviewed our institutional (Mayo Clinic Rochester) database on all patients admitted for salicylate intoxication during a three-year period (Jan. 2010-Sep. 2012). Twenty-two patients were admitted for acute salicylate intoxication (defined as an initial salicylate level >20 mg/dL). Among them, fourteen individuals had abnormally reduced anion gap or positive anion gap (Anion Gap: -71 to 3, Mean: -21.89, Std. Dev. 27.64) associated with elevated salicylate levels, (Salicylate level 24.5-75.4 mg/dL, Mean: 42.6 mg/dL, Std. Dev 14.7) elevated serum chloride concentration (Cl<sup>-</sup>: 97-198 mmol/L, Mean: 125, Std. Dev. 27) in the setting of acute metabolic acidosis (15-28 mmol/L, Mean HCO<sub>3</sub><sup>-</sup>: 23, Std. Dev. 3.3). Their serum albumin level was within, so were their serum calcium, magnesium, and phosphorus levels. None of them had paraproteinemia. There were no other identifiable causes of hyperchloremia or decreased anion gap. By using an alternative measurement system (Roche Cobas 6000, 8000), the Cl and AG were normal on the same blood specimen in twelve cases (the other two cases were not re-measured using the alternative method on the same samples). Further in vitro experiments suggested that salicylate interferes with Cl<sup>-</sup> measurement when using the standard Roche Integra instrument.

This study suggests that circulating supra-therapeutic levels of salicylate can interfere with Cl measurement by a routinely used Cl measurement technique, resulting in an abnormally reduced or positive AG metabolic acidosis. In patients presented with acute metabolic acidosis, abnormally reduced AG or positive AG can be associated with acute salicylate intoxication; low AG in this particular setting is spurious.

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## 16. Prevalence of Acute Kidney Injury in Mexican Patients With Sepsis, Severe Sepsis or Septic Shock. A Multi-Center Cohort Study

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<sup>1</sup>Instituto Mexicano del Seguro Social, <sup>2</sup>Secretaria de Salud, <sup>3</sup>ISSSTE

Introduction: Severe sepsis is one of the most common causes of admission to the intensive care unit (ICU) with a high rate of multi-organ failure and death. Acute kidney injury (AKI) is commonly observed in severe sepsis with a high associated mortality rate. The aim of this study was to determine the prevalence of AKI in Mexican patients suffering from sepsis, severe sepsis or septic shock.

Material and Methods: Data from ICU patients cohort study, from Mexican major teaching hospitals, were used as to determine prevalence of AKI in patients with sepsis, severe sepsis and septic shock. Independent variables were: gender, age, three groups of age were categorized (younger than 40 years, from 40 to 64.9 years and 65 and older), presence and /or absence of multi-organ failure (according to the Brussels scale). Dependent variables were: Presence or absence of AKI (according to the Brussels Scale with serum creatinine superior or equal to 1.5 mg/dL) and ICU and hospital mortality. Results: 3798 patients with sepsis, severe sepsis or septic shock were registered. 47.5% were male, with mean age of 53.1



years. Patients with AKI were older (49.4 vs. 56.59 years). Prevalence of AKI in severe sepsis/septic shock was 68.2%. Female had higher prevalence than men (72.5% vs. 63.6%). Age groups had a direct relationship with AKI. Indeed, older age had a higher prevalence of AKI (55.5%, 69.4% and 76.9%, respectively). Hospital mortality was 51.5% and associated mortality in AKI was 56.5%. Patients with AKI had higher mortality in ICU than patients without AKI (36.0% vs. 51.6%). Conclusion: Prevalence of AKI in sepsis, severe sepsis or septic shock is associated with higher mortality. Mortality is higher in female than men in our cohort. Older age is associated with a high mortality rate. Our incidence of AKI in sepsis, severe sepsis or septic shock is higher than reported previously in the literature (close to 70 %).

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## **17. Evaluation of the Postoperative State as a Predictor of Cardiac Surgery-Associated Severe Acute Kidney Injury**

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*Instituto Nacional de Cardiología, Ignacio Chavez*

Background: Cardiac surgery-associated acute kidney injury (CSA-AKI) has high morbidity and mortality. The usefulness of the postoperative state as a predictor of CSA-AKI is currently unknown.

Aim: To evaluate the utility of postoperative clinical status as predictor of CSA-AKI by it-self and in conjunction to preoperative risk factors.

Methods: Prospective cohort study including adult patients who underwent cardiac surgery between March 1st 2011 and June 29th 2012 at Instituto Nacional de Cardiología. Variables were registered before, during and after surgery.

Main outcome: Severe CSA-AKI was defined as AKIN 2/3 or RIFLE I/F according to serum creatinine and urinary output during the 7 days following surgery.

Results: 371 patients were included; of which 214 were men (57.5%). Median age was 56 (45-66), Euroscore was 4 (3-6) and glomerular filtration rate (GFR) was 81.2ml/min/1.73 m<sup>2</sup> (66.5-98.1). A total of 58 patients (15.6%) developed severe CSA-AKI.

After adjustment, postoperative variables found to be significantly associated to severe CSA-AKI were: reintervention/bleeding (OR 3.79 [1.46-9.83], p<0.006), diuretic use during surgery OR 3.57 [1.60-7.95], p<0.002), use of vasopressors at 24 hrs after cardiac surgery (OR 5.34 [2.11-13.49], p<0.001), CVP >16cmH<sub>2</sub>O (OR 2.694 [1.37-5.29], p<0.004) and low cardiac output (OR 2.21 [1.01-4.82], p<0.47). Those variables were compared to SOFA and APACHE scores with areas under the curve (AUC) not reaching statistical significance among them (0.77 vs 0.73 and 0.72, respectively, p=0.428).

Finally, we add the postoperative score to the preoperative risk and it was possible to classify our population in four-category risk for CSA-AKI, very high, high, intermediate and low risk for AKI (95.7, 29.6%, 15.4 and 3.7%, respectively) as early as 24 hours after cardiac surgery. We noticed that a high postoperative score led to a high risk for severe CSA-AKI independently of preoperative risk score.

Conclusion: Postoperative status is highly associated with the risk of severe CSA-AKI. The addition of postoperative evaluation to preoperative risk can classify patients into 4 risk categories, which could help to create algorithms for prevention and treatment of CSA-AKI.

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## **18. Adenoviral Infection Cleared Via Intravenous Cidofovir Treatment in Two Children on Continuous Veno-venous Hemodiafiltration**

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Adenoviral (AV) infections severely complicate the care of critically ill, immunosuppressed patients (pts), but can be treated with intravenous (IV) cidofovir (CV), a broad-spectrum antiviral with minimal protein binding and near complete kidney elimination. Active metabolite may persist for extended periods, so prolonged interval dosing has been reported for pts with kidney dysfunction, including hemodialysis (HD) pts; however no dosing recommendations exist for pts treated with

continuous veno-venous hemodiafiltration (CVVHDF). We present two children treated with IV CV for AV infections during CVVHDF.

A 5 yr old girl with relapsed T-cell leukemia underwent bone marrow transplantation (TX) complicated by sinusoidal obstruction syndrome (SOS) and multiple infections (cytomegaloviremia, BK viruria, and disseminated AV) leading to multi-organ failure. Pt required CVVHDF for acute kidney injury (AKI) from abdominal compartment syndrome (ACS) due to SOS-related ascites and multiple nephrotoxic medications. CV was dosed 1 mg/kg thrice weekly at start of CVVHDF, and then increased to 1.5 mg/kg q 48 hrs for rising serum AV PCR titers. Pt transitioned for 10 days to HD, and CV was dosed 1 mg/kg after each treatment. Pt restarted CVVHDF for hemodynamic instability, so IV CV 1.5 mg/kg resumed. After increased CV on CRRT, 16 days later serum and urine AV PCR levels became undetectable and decreased in stool. Unfortunately, pt's disease burden worsened and she passed.

A 2 yr old boy with biliary atresia underwent liver TX post-operatively complicated by cardiac arrest, hepato-renal syndrome (HRS), and AV viremia/enteritis. Pt required CVVHDF for AKI from poor kidney perfusion during cardiac arrest, ACS due to HRS-induced ascites, and multiple nephrotoxic medications. Prior to initiating CVVHDF, pt was first treated with CV 0.6 mg/kg thrice weekly, with decreasing serum AV PCR titers. After CVVHDF was begun, CV dosing was continued 1.5 mg/kg q48 hours. After 13 days CV therapy, pt's serum AV PCR titers were negative, as well as stool. After 3 weeks of therapy, CV was stopped with no relapse of infection. Pt's AKI never recovered enough to discontinue RRT; however he was transitioned to HD and discharged home.

These two cases show AV may be cleared with IV CV 1.5 mg/kg q48 hours while on CRRT. Further evaluation by studying CV pharmacokinetics is planned.

## 19. Improved Acute Kidney Injury (AKI) Staging Criteria for Predicting Hospital Mortality Across Demographic Strata

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The objective of this study is to optimize AKI staging strategies across demographic strata, with inpatient survival as the primary endpoint. Several approaches for staging AKI have been described (RIFLE, AKIN and KDIGO), and the insensitivity of the RIFLE criteria for staging AKI in elderly patients has recently been noted (Chao et al. Kid Int 82:920, 2012). We have developed a simplified AKI Staging approach, using time-dependent hazard ratios (TDHR) and absolute changes in [sCr], similar to that originally described by Chertow et al (JASN 16:3365, 2005), and now apply this Delta-Creatinine analysis to age-, race- and gender-stratified regression models. The table shows classification of significant (Yes) or lack (No) of discrimination between AKI stages for inpatient mortality following maximum increases in serum creatinine over the initial inpatient baseline values.

The Delta-Creatinine approach outperformed other classification schemes, including the recent KDIGO Workgroup Consensus Criteria (Kid Int Suppl 2:1, 2012), for predicting in-patient hospital mortality at a single tertiary referral academic medical center (Wang et al NDT, in press, 2013). With stratification for demographic factors, we now report that the Delta-Creatinine approach provides significant discrimination between AKI stages for predicting in-patient mortality across all strata. The RIFLE criteria did not differentiate any risk gradient between Stage 2 and Stage 3 for any strata.

Conclusion: A robust, simplified approach has been developed for AKI staging using absolute increases in [sCr] and TDHR analysis. This approach performs well for age and other demographic strata, and demonstrates novel criteria for selecting optimal AKI staging cut-points for all demographic strata.

	Strata	Stage 0 and Stage 1	Stage 1 and Stage 2	Stage 2 and Stage 3
RIFLE/DELTA_CREATININE	ALL	YES/YES	YES/YES	YES/YES
RIFLE/DELTA_CREATININE	AGE >65 YEARS	YES/YES	YES/YES	NO/YES
RIFLE/DELTA_CREATININE	MALES	NO/YES	YES/YES	NO/YES
RIFLE/DELTA_CREATININE	BLACKS	YES/YES	YES/YES	NO/YES

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## RESEARCH IN AKI

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### 20. Effects of nafamostat on continuous renal replacement therapy for critically ill patients at high risk of bleeding

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Continuous renal replacement therapy (CRRT) has emerged as the preferred dialysis modality for critically ill patients with acute kidney injury, particularly those with hemodynamic instability. Anticoagulation is necessary for effective delivery of CRRT, but this requirement can also present challenges, as many critically ill patients with sepsis and inflammation already have a higher risk of bleeding as well as clotting. This retrospective study has been to assess the effect of nafamostat on circuit patency and the safety about bleeding complication in patients at high risk of bleeding. We investigated 243 patients undergoing CRRT at high risk of bleeding. We started CRRT without anticoagulation, and nafamostat was used if hemofilter lifespan was less than 12 h. The average hemofilter lifespan was measured before and after drug infusion to evaluate the efficacy of nafamostat. The frequency and number of red blood cell (RBC) transfusions were measured to assess the safety of nafamostat. 62 (25.5%) patients received nafamostat. In nafamostat group, the hemofilter lifespan was lengthened from 10.2 (7.5–13.0) h to 19.8 (12.6–26.6) h after druginfusion ( $p < 0.001$ ). The hemofilter lifespan was 27.5 (17.5–38.2) h in anticoagulation-free group. The frequency of RBC transfusion during CRRT did not differ between the nafamostat group and the anticoagulation-free group (71%vs. 70%,  $p = \text{NS}$ ). The median RBC units transfused per CRRT day was also not different between the two groups [0.7 (0.5–1.0) units/day vs. 0.7 (0.4–1.1) units/day;  $p = \text{NS}$ ]. Use of nafamostat in CRRT for patients at high risk of bleeding lengthened the filter survival time without an increase in RBC transfusion.

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### 21. Effects of Combination of Hydroxyethyl Starch and 0.9% Saline On Endothelial Injury In a Rabbit Model of Crush Syndrome

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Background Crush syndrome is common injury after the earthquake, collapse and other disasters, acute kidney injury and vascular endothelial injury are major component of crush syndrome. Fluid resuscitation is a key to prevention and treatment of acute kidney injury, but what kind of crystalloid-colloid is more appropriate currently surviving in the debate. Because Hydroxyethyl starch (HES) can reduce the endothelial damage and have few side effects on kidney function. We compared the combination of 6% HES 130/0.4 with 0.9% saline and 0.9% saline alone treatment of Crush syndrome , to observe the effect of two treatment options on endothelial damage after crush injury.

Method In the study, crush syndrome model was made by a specific extrusion equipment to establish a rabbit model of severe crush syndrome. 24 male New Zealand rabbits were randomly assigned to four groups: Sham Group (n=6), not crushed; Model Group (n=6), both hindlimbs of rabbits were compressed for 6h with 36 times the weight; SAL Group (0.9% saline, n=6); SAL/HES Group (the combination of 0.9% saline and 6% HES 130/0.4, n=6). Fluid resuscitation target maintained a mean arterial blood pressure of 65 mm Hg initiated 60 min before the end of the crush period. Some tests such as serum Cr , BUN ,Ca2 + , CK, and urine endothelial cell-specific molecular-1, KIM-1,NGAL ,IL-6, IL-10, were performed at 24 h post-resuscitation.

Result Compared with Sham group , the level of serum Cr , BUN , CK, AST, ALT and K<sup>+</sup> were increased in Model group at

the end of observation, but the level of  $\text{Ca}^{2+}$  was decreased ( $p < 0.05$ ); Urine NGAL and KIM-1 levels were significantly increased ( $p < 0.05$ ) from reperfusion for 3 hours, 6 hours onwards increased. After treatment of 6% HES 130/0.4 and 0.9% saline or 0.9% normal saline alone rehydration at the end of the experiment, we found the serum Cr, BUN, CK, AST, LDH,  $\text{K}^{+}$  and urine KIM-1, NGAL level were lower in the SAL / HES group and the SAL group than in Model group ( $p < 0.05$ ); Compared with Model group, the serum IL-6 and IL-10 were also decreased in the SAL / HES group and the SAL group ( $p < 0.05$ ).

**Conclusions** The combination of 6% HES 130/0.4 with 0.9% saline resuscitation may prevent acute kidney injury at early stage of Crush syndrome by alleviating endothelial damage, modulating systemic inflammatory response.

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## 22. The Relationship between Acute Kidney Injury and Brain MRI Findings in Asphyxiated Newborns after Therapeutic Hypothermia

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**Background:** Therapeutic hypothermia has become the standard of care for asphyxiated newborns. The impact of acute kidney injury (AKI) on brain MRI findings in asphyxiated newborns following therapeutic hypothermia has not been studied. We hypothesized that hypoxic-ischemic lesion on brain MRI would differ between infants with AKI compared to those without AKI following cooling.

**Design/Methods:** Medical records of 88 consecutively cooled infants who had brain MRI were reviewed. All infants had creatinine at start baseline (initiation of cooling); at 24, 48, and 72h; and then on day 5 or 7 of life. A neonatal modification of the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines were used to classify AKI. The MRI images were evaluated for hypoxic-ischemic injury by a neuroradiologist, who was masked to clinical parameters and outcomes. Injuries to both basal ganglia/thalamus and cortex were considered severely abnormal. Multivariate analysis determined if any of the pre-cooling variables (e.g. Apgar score, cord pH and base deficit, neurologic examination, etc.) to assess the severity of asphyxia or the presence of AKI predicted the primary outcome of an abnormal MRI.

**Results:** AKI was found in 34 (39%) of 88 infants with 15, 7, and 12 fulfilling criteria for stage I, II, and III, respectively. Brain MRI abnormalities related to hypoxia-ischemia was present in 50 (59%) infants. In 26 infants (AKI 14, no AKI 12), MRI was severely abnormal. Abnormal MRI was more frequent in infants from the AKI group (AKI 25 of 34, 73% versus No AKI 25 of 54, 46%,  $p = 0.012$ , OR 3.2, 95% CI 1.3-8.2). However, severely abnormal MRI was similar between the two groups ( $p = 0.091$ ). Multivariate analysis identified only that AKI ( $p = 0.032$ , OR 2.9, 95% CI 1.1-7.6), and chest compression during resuscitation were independently associated with the primary outcome.

Severely abnormal MRI in infants with stage III AKI was not different compared to infants with stage II (stage III AKI 3 of 12, 25% versus stage II AKI 3 of 7, 43%;  $p = 0.617$ ) or stage I AKI (stage III AKI 3 of 12, 25% versus stage I AKI 8 of 15, 53%;  $p = 0.238$ ).

**Conclusions:** The present study emphasizes the importance of recognizing AKI in asphyxiated newborns receiving therapeutic hypothermia, and offers insights into the potential differential beneficial effects of hypothermia on brain and kidney. AKI is independently associated with the presence of hypoxic-ischemic lesions on post-cooling brain MRI.

### 23. Treatment of the rhabdomyolytic acute kidney injuries with plasma exchange and continuous veno-venous haemofiltration

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**Introduction:** Rhabdomyolysis is a pathogenic cause of acute kidney injury in a large number of cases where traumatic or non-traumatic causes induce muscle cell disruption. Myoglobin has a molecular mass of 17 kDa but because it is not-spherical and carries electrical charges it can be considered to be a solute with an Einstein-Stokes radius greater than expected. In these circumstances, not only does the solute have a very low diffusion coefficient, thus requiring transport by convection, but it also possesses a steric magnitude that is likely to be rejected by the membrane pores.

**Material & Methods:** Three patients with traumatic rhabdomyolysis and seven – with non-traumatic were treated with plasma exchange (PEX) at average volume of 2 500 ml per procedure at 48 hour interval. We used fibrillar plasma filter with effective area 0,3m<sup>2</sup>. Substitution was performed with 4% solution of human albumin in buffer. Continuous veno-venous haemofiltration (CVVH) was performed in “PEX free” periods at average continuity of 8 hours. We used hyperpermeable haemofilter for CRRT. The procedures were effected with “Diapact” CRRT unit. We took advantage of units’ mobility and its independence of re-osmotic water. For myoglobine detection in the serum we used immuno-chemic analyzer IMMULITE. The unit works on combine principle – both on enzyme marking and semi-luminescent detection.

**Results:** In both groups we observed initial extremely high levels of myoglobine in serum- over 800 ng/ml ( N- 2,6-70 ng/ml). In the end of treatment all patients have restored or stabilized their renal function. Levels of myoglobine were under 120 ng/ ml.

**Conclusions:** The usage of PEX is resulting in high level of “sieving” coefficient, but the result clearance is insufficient because of the imposed restrictions in the volume of exchanged plasma. To correct this disadvantage we use continuous veno-venous haemofiltration.

Finally, the membrane and technique used for the membrane separation process are crucial for the efficiency of the therapy. There is no question that convection should be used, because of the molecular mass of the solute. However, standard cellulosic membranes are practically impermeable to the molecule: high-flux membranes should be used.

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### 24. Effect of Daytime High Volume Hemofiltration Therapy in Sepsis Patients with Acute Kidney Injury

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**Objective** To study the effect of daytime high volume hemofiltration(HVHF) in sepsis patients with acute kidney injury. **Methods** 30 patients were divided randomly into two groups, HVHF or continous vein-vein hemofiltration(CVVH)group. In HVHF group, Blood flow is 220-250ml per minute. replacement fluid is 6L/h, total replacement fluid is 48-60L each day. While in CVVH group, Blood flow is 180-220ml per minute.replacement fluid is 2-4L/h , total replacement fluid is 48-60L each day. Serum creatinine、BUN、electrolyte and CO2CP was measured before and after treatment. Serum TNF $\alpha$ 、IL-1 $\beta$ 、IL-6 were measured before and 4h,8h,12h after treatment. The Severity of illness were evaluated by APACHE II (Acute Physiology and Chronic Health Evaluation II), organ dysfunction/failure described by The SOFA (Sepsis-related Organ Failure Assessment).Results In HVHF group, 12 cases survived and mortality rate was 20% , in CVVH group, only 6 cases survived and mortality rate was 60%. Difference of mortality between two group was Statistically significant (p<0.05). Patients in two groups showed stabled dynamics and favorable change of creatinine、BUN、electrolyte and acid-base balance. Serum TNF $\alpha$ 、IL-1 $\beta$  and IL-6 decreased significantly in HVHF group than in CVVH group(p<0.05). **Conclusion**

Daytime HVHF can effectively remove extra solute, and adjust ionic and acid-base balance, and eliminate inflammatory cytokines to improve the prognosis of sepsis patients.

Table 1. serum level of cytokine TNF $\alpha$ , IL-1 $\beta$ , IL-6 change in two group patients ( ng/L )

group	Pre-treatment			4h after treatment			8h after treatment			12h after treatment		
	TNF- $\alpha$	IL-1 $\beta$	IL-6	TNF- $\alpha$	IL-1 $\beta$	IL-6	TNF- $\alpha$	IL-1 $\beta$	IL-6	TNF- $\alpha$	IL-1 $\beta$	IL-6
HVHF	1845 $\pm$ 613	1072 $\pm$ 136	1404 $\pm$ 415	1260 $\pm$ 395 <sup>△</sup>	520 $\pm$ 113 <sup>△</sup>	794 $\pm$ 452 <sup>△</sup>	1453 $\pm$ 373 <sup>△</sup>	716 $\pm$ 84 <sup>△</sup>	863 $\pm$ 243 <sup>△</sup>	1550 $\pm$ 373 <sup>△</sup>	420 $\pm$ 74 <sup>△</sup>	878 $\pm$ 210 <sup>△</sup>
CVVH	1859 $\pm$ 742	1099 $\pm$ 243	1440 $\pm$ 412	1543 $\pm$ 639/	757 $\pm$ 324	785 $\pm$ 364 <sup>△</sup>	1748 $\pm$ 732	940 $\pm$ 225	1230 $\pm$ 381	1665 $\pm$ 462/	970 $\pm$ 238	1540 $\pm$ 403
F value	0.965	0.847	0.864				1.932	2.874	2.56	1.842	0.740	2.32
P value	0.060	0.05	0.055	1.8752	1.170	1.173	0.020	0.010	0.015	0.0155	0.06	0.023
				0.0300	0.016	0.035						

<sup>△</sup>refers to compared with pre-treatment, P value is less than 0.05.

## 25. Bicarbonate Based Solutions in the Management of Acute Kidney Injury

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**Background:** Fluid administration constitutes an important part of the treatment of established acute kidney injury (AKI). Optimization of the hemodynamic status and correction of any volume deficit helps to minimize further extension of AKI, and facilitates recovery from AKI. The optimal hydration strategy for management AKI remains unknown. AKI is often associated with acidosis. Acidosis has been linked to several adverse effects that are deleterious to kidney function; it has been shown to increase interleukine production and endothelin secretion. We hypothesized that the use of bicarbonate-based solution will facilitate the recovery from AKI. **Methods:** We analyzed data from 59 hospitalized patients from a University based hospital; who developed AKI. Patients with CKD K-DOQI stages 4 and 5 were excluded. Twenty-nine patients received bicarbonate-based solutions for the management of AKI and thirty patients received different types of bicarbonate-free solutions (saline, half-saline, ringer lactate, or colloids). We assessed the effect of bicarbonate-based solutions on delta serum creatinine (sCr), urine output, days to achieve basal sCr, and the amount of fluids been administered on each group. **Results:** Of the 59 patients included in this study, 29 patients received bicarbonate-based solutions and 30 patients received other types of I.V. fluids. Median baseline sCr was higher in the patients who received bicarbonate-based solutions (1.12 IQR[0.9 – 1.3] vs. 1.08 IQR[0.9 – 1.23] mg/dL;  $p < 0.001$ ). sCr reduction rate was higher in the group treated with bicarbonate-based solution (mean  $\Delta$  sCr -0.29  $\pm$  0.47 vs. -0.07  $\pm$  0.42 mg/dL;  $p = 0.007$ ). Patients in whom bicarbonate based solutions returned to their baseline sCr in fewer days (5.6  $\pm$  2.1 vs. 7.6  $\pm$  2.8 days;  $p < 0.001$ ). No difference was found in 24 hr urine output between patients who received bicarbonate-based solutions and those who received other types of solutions (1,592 IQR[1,409 – 1,905] vs. 1,647 IQR[1,296 – 2,192] ml;  $p = 0.294$ ); no difference also was found in the amount of fluids that each group received (bicarbonate-based 1,000 IQR[500 – 2,000] vs. bicarbonate-free 1,000 IQR[1,000 – 2,000] ml;  $p = 0.903$ ). **Conclusions:** Bicarbonate-based solutions for the treatment of established AKI could improve renal function, accelerating renal recovery. An adequately powered randomized controlled trial is warranted to support the use of bicarbonate-based solution in patients with AKI.



## 26. Urinary cystatin C levels as a diagnostic and prognostic biomarker in patients with acute kidney injury

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**Introduction.** Acute kidney injury (AKI) is a frequent complication in critically ill patients and is associated with a high mortality and morbidity. Clinicians have limited tools to predict the course of AKI at the time of serum creatinine increase. Several novel urinary biomarkers including neutrophil gelatinase-associated lipocalin (NGAL), cystatin C (CyC), and kidney injury molecule-1 (KIM-1) have been proposed for the early detection of injury or prediction of outcome, but only few data regarding the use of biomarkers to detect tubular injury and predict the clinical course at the time of AKI diagnosis are available. We evaluated the diagnostic and prognostic utility of urinary cystatin C (uCysC) in patients with AKI.

**Methods.** In this study, serum and uCysC and urinary creatinine (uCr) were measured in patients presenting with acute kidney injury. The patients were divided into two groups; those with prerenal AKI and those with intrinsic AKI. Prerenal AKI was defined as a new-onset increase in serum creatinine (sCr) that resolved within 72 hours and returned to the baseline kidney function level. Patients with intrinsic AKI were defined and classified according to the Acute Kidney Injury Network (AKIN) criteria.

**Results.** Of the total number of patients (n = 213), 40.4% (n = 86) were judged to have prerenal AKI and 59.6% (n = 127) intrinsic AKI. uCysC levels and the uCysC/uCr ratio were significantly higher in intrinsic AKI versus prerenal AKI. Intrinsic AKI was defined and classified according to the Acute Kidney Injury Network (AKIN) criteria; 39 (37.7%), 37 (29.1%), and 51 (40.2%) patients were assigned to stages 1, 2, and 3, respectively. In intrinsic AKI, the uCysC concentration increased according to AKI severity. The uCysC/uCr ratio was significantly higher in the RRT group versus the non-RRT group (0.15 vs. 0.08, respectively; p = 0.037). In a multivariate analysis, the uCysC/uCr ratio was associated with in-hospital mortality (p = 0.019).

**Conclusion.** uCysC level and the uCysC/uCr ratio were useful biomarkers of intrinsic AKI, and the uCysC/uCr ratio was valuable predictor of in-hospital death in AKI patients.

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## 27. Hepatic Injury Secondary to Renal Ischemia-Reperfusion (I/R) Injury: Possible Role of Nitric Oxide

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**BACKGROUND and AIM:** Nitric oxide (NO) is an important mediator of the physiological and pathological processes such as renal ischemia/ reperfusion (I/R) injury. There remains continuing uncertainty about the role of NO in renal I/R injury with theoretical and experimental evidences offering support for both toxic and protective role. So, the aim of this study is to declare the probability of liver affection consequent to renal I/R and to study the role of NO (toxic or protective) in the pathogenesis of this probable hepatic affection.

**MATERIALS and METHODS:** 48 Sprague-Dawley rats, weighing from 250-300 grams, aging 4-6 months are divided randomly into 4 equal groups. Group I (Sham-operated), Group II (I/R injury), Group III (I/R injury with administration of L-arginine; 300 mg/kg IV 20 min before ischemia), Group IV (I/R injury with administration of N- omega-nitro-L-arginine methyl ester (L-NAME); 50 mg/kg in IV 20 min before ischemia). Kidney functions tests [KFTs](serum creatinine and BUN), liver enzymes (ALT, AST) were measured at 2 hrs after ischemia. Malondialdehyde (MDA), catalase, reduced glutathione (GSH) and NO were examined at 2 hrs after ischemia in frozen section samples of the liver tissues. Histopathology (H&E stain) of the liver was examined by a specialized pathologist.



**RESULTS:** Group II showed significant increase in [KFTs] and Liver enzymes but without any change in liver histopathology by light microscope in comparison to Group I ( $p < 0.001$ ). Administration of L-arginine significantly worsened the liver enzymes and histological parameters ( $p \leq 0.028$ ) with improvement of the kidney functions tests ( $p \leq 0.007$ ) in comparison to Group II. Moreover, administration of L-NAME caused significant and marked worsening of liver enzymes and liver histopathology in comparison to Group II ( $p \leq 0.008$ ). When the liver from Group II compared to Group I it showed significant decrease in MDA and increase in GSH and NO ( $p \leq 0.001$ ). L-arginine group showed significant decrease in GSH and catalase and significant increase in NO and MDA in comparison to Group II ( $p < 0.001$ ). L-NAME group showed significant increase in MDA and decrease in NO and GSH in comparison to Group II also ( $p < 0.001$ ).

**CONCLUSION:** Endogenous NO has a protective effect against hepatic injury induced by renal I/R injury, while exogenous NO by L-arginine worsens the hepatic injury induced by renal I/R injury. This probably is due to increased formation of reactive oxygen species.

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## **28. Macrophage Stimulating Protein (MSP) Promotes Tubular Regeneration And CD133+ Renal Progenitor Cell Differentiation After Kidney Ischemia-Reperfusion Injury (IRI)**

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**Background and aim of the study:** Delayed graft function (DGF) is an early complication of kidney transplantation (KT) mainly due to ischemia-reperfusion injury (IRI). MSP is a plasminogen-related growth factor able to induce tubular proliferation after binding to its specific tyrosine-kinase receptor named RON. The aim of this study was to define the potential role of the MSP-RON pathway in kidney regeneration after IRI in the setting of DGF.

**Methods:** Plasma and urine levels of MSP were evaluated by ELISA before and the first week after KT. Data were correlated with plasma NGAL, a known biomarker of DGF. Immunohistochemistry for MSP and RON was performed at different time points on kidneys of male Wistar rats subjected to renal IRI. In vitro, we evaluated the effects of MSP on human tubular cells subjected to hypoxia (proliferation, apoptosis, cell polarity) and on the differentiation of CD133+ renal progenitor cells.

**Results:** At day 2 after transplantation, plasma and urine levels of MSP were higher in patients with immediate graft function (IGF) in respect to patients with DGF (plasma IGF  $7.42 \pm 0.98$  ng/ml vs. plasma DGF  $1.98 \pm 0.44$  ng/ml; urine IGF  $1.24 \pm 0.31$  ng/ml vs. urine DGF  $0.19 \pm 0.05$  ng/ml). In IGF patients, the increase of MSP levels peaked at day 2 in concomitance to the decrease of plasma NGAL, indicating the recovery of renal function. In the experimental model of renal IRI in rats, a significant up-regulation of MSP and RON was observed in tubular epithelial cells in the regenerative phase after IRI (day 5). In vitro, we observed an increased expression and release of MSP from TEC cultured under hypoxia. In hypoxic TEC, MSP induced proliferation, preservation of cell polarity and resistance to apoptosis through the inhibition of both death receptor (Fas) and mitochondrial (Bcl-XL/Bcl-2) pathways and caspase-3, -8 and -9 activation. In addition, MSP induced CD133+ progenitor cells expressing RON to proliferate and to differentiate into mature epithelial cells, acquiring cell polarity and a tubular-like-phenotype confirmed by the expression of E-cadherin, megalin, alkaline phosphatase, aquaporin-1 and NGAL.

**Conclusions:** MSP promotes tubular regeneration and CD133+ renal progenitor cell differentiation following IRI through a paracrine mechanism. MSP may be envisaged as potential therapeutic approach for DGF after KT. Further studies are needed to define the role of MSP as potential biomarker of IGF/DGF.

## **29. Microvesicles Derived From Endothelial Progenitor Cells Protect From Antibody- And Complement-Mediated Endothelial Injury Through Transfer Of Specific mRNAs and microRNAs**

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**Introduction and aim of the study:** Antibody-mediated rejection (ABMR) is one the main causes of acute kidney graft failure due to complement-mediated endothelial injury following antibody ligation, in particular in presence of anti-HLA donor specific antibodies (DSA). Endothelial progenitor cells (EPCs) are known to promote tissue repair by paracrine mechanisms including the release of microvesicles (MVs), small particles able to induce epigenetic reprogramming of target cells through RNA transfer. The aim of this study was to evaluate whether MVs derived from EPCs may prevent antibody- and complement-mediated endothelial injury.

**Methods:** EPCs were isolated from peripheral blood and MVs were collected from supernatants of cultured EPCs by ultracentrifugation and characterized for protein and RNA content. The biological effects of MVs were evaluated on human glomerular-derived (HGECS) or porcine aortic (PAECs) endothelial cells cultured in presence of plasma drawn from DSA-positive kidney transplanted patients or of anti-Gal antibodies, respectively.

**Results:** MV analysis revealed the presence of pro-angiogenic and anti-apoptotic molecules (eNOS, P-Akt, Bcl-XL), complement inhibitors (Factor H, CD55, CD59) and enrichment for microRNAs including the pro-angiogenic miR-126 and miR-296. MVs were efficiently internalized in HGECS as well as in PAECs. In HGECS incubated with DSA-positive plasma, MVs promoted angiogenesis and inhibited apoptosis, lymphocyte adhesion (particularly NK cells) and expression of E-selectin, VCAM-1 and CD40 on endothelial cell surface. Similar results were observed in anti-Gal-stimulated PAECs, where mRNAs coding for human Factor H, CD55 and CD59 were detected after stimulation with MVs. These results were not observed when MVs were treated with RNase or using MVs derived from EPCs subjected to knock-down of Dicer, the intracellular enzyme essential for microRNA synthesis, or transfected with siRNA directed to the complement inhibitors Factor H, CD55 and CD59.

**Conclusions:** MVs derived from EPCs protect from antibody- and complement-mediated endothelial injury by delivering their RNA content. The mRNA/microRNA cargo of MVs was shown to contribute to reprogramming injured endothelial cells toward a regenerative program due to complement inhibition and triggering of angiogenesis, suggesting a potential role of EPC-derived MVs in the mechanisms of graft accommodation.

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## **30. Nafamostat Mesilate as Anticoagulant During Continuous Renal Replacement Therapy in The Patients with High Risk of Bleeding: A Randomized Prospective Study of Nafamostat Mesilate versus no Anticoagula**

Jang- Hee Cho<sup>1</sup>, Yun Jeong Kang<sup>1</sup>, Ga-Young Park<sup>1</sup>, Jun-Seop Kim<sup>1</sup>, Owen Kwon<sup>1</sup>, Ji-Young Choi<sup>1</sup>, Sun-Hee Park<sup>1</sup>, Yong Lim Kim<sup>1</sup>, Chan Duck Kim<sup>1</sup>

<sup>1</sup>*Kyungpook National University Hospital, Daegu, Korea*

**Background:** Nafamostat mesilate, a synthetic serine protease inhibitor, has been widely used in Korea as an anticoagulant during continuous renal replacement therapy (CRRT). However, there were limited data from randomized study of nafamostat mesilate in acute kidney injury (AKI) patients with bleeding tendency. This prospective study evaluated the efficacy and safety of nafamostat mesilate in CRRT for patients with AKI who were at high risk of bleeding.

**Methods:** From July 2008 to June 2012, patients with AKI were randomized to receive nafamostat mesilate (NM group) or normal saline (control group) as an anticoagulant during CRRT. Patients who fulfilled one of the following criteria were defined as high risk of bleeding: spontaneous bleeding, aPTT >45 sec, PT >17 sec, thrombocytopenia, and recent surgery. Primary outcome was to compare treatment efficacy represented by hemofilter life span. Several parameters of safety and

efficacy were analyzed as secondary outcomes.

Results: Fifty five patients were included in the study (NM group=31, control group=24). The baseline characteristics were

not significantly different between the two groups. The mean hemofilter life span was  $29.8 \pm 23.0$  hrs in the NM Group which was significantly longer than  $19.5 \pm 14.9$  hrs in the control group ( $p=0.001$ ). The most common cause of filter failure was filter clotting which showed higher tendency in control group than in NM group (56.1% vs. 37.7%,  $p=0.059$ ). There were no significant differences in transfusion and major bleeding between groups. The patient survival rates of NM group at 30 days and 90 days after initiation of CRRT were comparable to those of control group.

Conclusion: Nafamostat mesilate could be used as anticoagulant during CRRT providing sufficient filter survival without additional risk of bleeding in critically ill AKI patients with bleeding tendency.

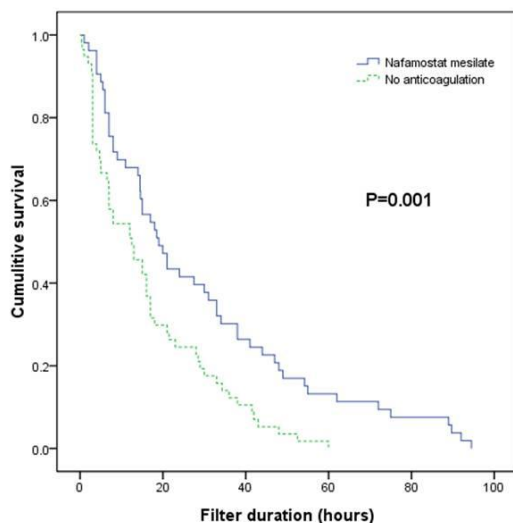


Figure1. Kaplan–Meier survival function indicating hemofilter survival times between nafamostat and no anticoagulation treatment group

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### 31. The EUPHRATES Trial (Evaluating the Use of Polymyxin B Hemoperfusion in a Randomized controlled trial of Adults Treated for Endotoxemia and Septic shock): A Blinded Theragnostic Hemoperfusion Trial

David J Klein<sup>1</sup>, Walker M Paul<sup>2</sup>, Foster Debra<sup>2</sup>, Marshall C John<sup>1</sup>, Schorr Christina<sup>3</sup>, Dellinger P R<sup>3</sup>

<sup>1</sup>St. Michael's Hospital, <sup>2</sup>Spectral Diagnostics Inc., <sup>3</sup>Cooper University Hospital

Background: Despite great advances in our understanding of the pathophysiology of sepsis, attempts to translate these findings into novel treatments and improved outcomes for patients have been disappointing. Recently, there has been renewed interest in hemoperfusion-based therapies targeting sepsis and reducing acute kidney injury (AKI). Success of these therapies requires better selection of patients in trials based on biology for specific treatments and rigorous methodology to validate results. Here we describe the EUPHRATES Trial as a multi-centered, blinded, pivotal, randomized controlled trial of Polymyxin B hemoperfusion (Toraymyxin) in patients with septic shock and confirmed endotoxemia using the Endotoxin Activity Assay (EAA). Methods: The trial is being conducted in sixty ICUs in the United States and Canada and aims to enroll 360 patients. Eligible patients must have vasopressor dependant septic shock, evidence of organ dysfunction, and an EAA in the high range of  $>0.60$ . The primary endpoint for the trial is a reduction in 28 day all-cause mortality. The trial has at least an 80% power to detect a 15% absolute difference in the primary endpoint. Secondary endpoints include reductions in AKI and improvements in hemodynamics as well as aggregate organ dysfunction score (MODS). Unique features of the trial include use of a detailed “fascade” hemoperfusion event as a blinding mechanism whereby patients randomized to the standard of care arm have two “façade” hemoperfusion events done and blinding is

maintained. No actual “sham” hemoperfusion is done. Two interim analysis are planned for the study – one after 76 patients for safety and one after approximately 180 patients. Results: As of April 2012, in a cohort of 103 evaluable screened patients, for those with an EAA <0.40 (low), 28 day mortality was 26%, for those with an EAA 0.40-0.59 (intermediate), 28 day mortality was 35%, and for those enrolled and randomized with an EAA >0.60 composite mortality (received treatment or sham) was 40%. With rare exceptions, blinding has been well maintained within the trial to date. Conclusions: The EUPHRATES trial is the first truly theragnostic trial targeting endotoxemia, septic shock, and AKI in this underserved high mortality patient population. Façade hemoperfusion is feasible as a blinding mechanism in a complex sepsis trial. Results are expected in approximately 2 years.

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### **32. Perioperative plasma NGAL measurement in LVAD implantation surgery**

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<sup>1</sup>*Department of Nephrology and Endocrinology, The University of Tokyo,* <sup>2</sup>*Department of Emergency and Critical Care Medicine, The University of Tokyo,* <sup>3</sup>*Department of Cardiothoracic Surgery, The University of Tokyo*

**Background:** Recently, implantation of left ventricular assist device (LVAD) has been widely conducted for the treatment of severe heart failure. Perioperative complication of end-organ injury including acute kidney injury (AKI) is a frequent and serious problem in LAVD implantation. Because serum creatinine (Scr) cannot be a good renal injury marker in AKI especially under dialysis, we evaluated an emerging biomarker plasma neutrophil gelatinase-associated lipocalin (NGAL), which can detect AKI before serum creatinine elevation, in a LVAD implantation cohort.

**Methods:** We prospectively studied 18 severe heart failure patients underwent LVAD implantation during the period of July 2011 to August 2012 at the University of Tokyo Hospital. Plasma NGAL was measured at pre-operation, just after operation, post-operative day (POD) 1, 7, 14, and 28. Diagnosis and severity of AKI was determined by the KDIGO creatinine criteria and severe AKI defined as stage 2 or 3.

**Results:** Causes of severe heart failure in this cohort were as follows; 9 idiopathic cardiomyopathy, 4 ischemic cardiac disease, 3 hypertrophic cardiomyopathy and 2 myocarditis. Fifteen (83%) patients were diagnosed as AKI and severe AKI occurred in 10 patients (6 patients were treated by dialysis). The severe AKI group showed higher plasma NGAL just after the surgery and at POD 1, 7, 14 compared with the non-AKI or mild AKI (stage 1) groups. In addition, severe AKI treated by dialysis showed higher plasma NGAL, while their Scr values were influenced by dialysis. Plasma NGAL just after the surgery showed a good performance for detecting severe AKI [AUC-ROC 0.87 (95%CI 0.61-0.96)].

**Conclusion:** Measurement of perioperative plasma NGAL will be useful for predicting severe AKI and especially when treated by dialysis in LVAD implantation surgery.

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### **33. Early initiation of continuous renal replacement therapy may improve patient survival in acute kidney injury**

Hark Rim<sup>1</sup>, Ye Na Kim<sup>1</sup>, Ho Sik Shin<sup>1</sup>, Yeon Soon Jung<sup>1</sup>

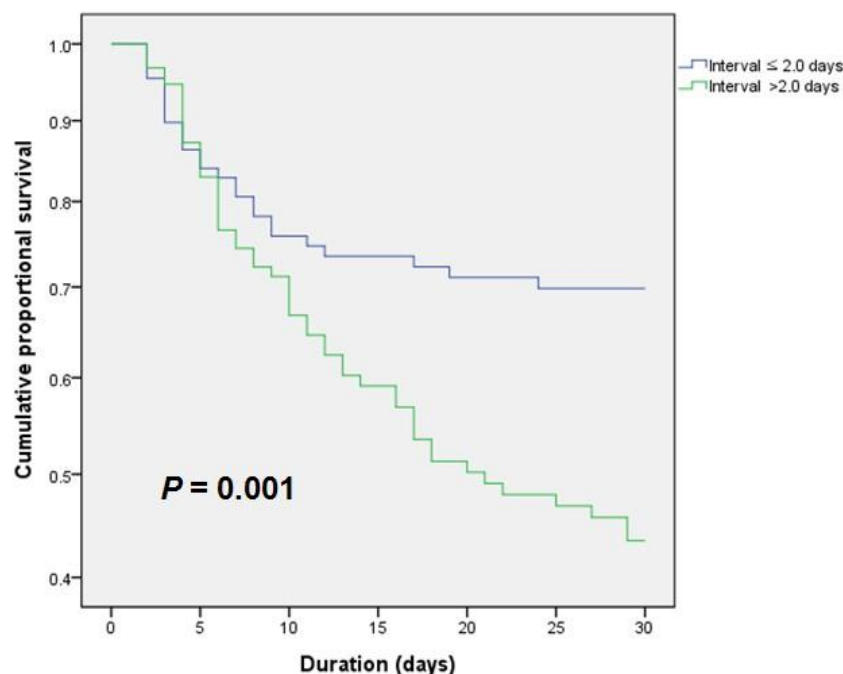
<sup>1</sup>*Kosin University College of Medicine*

**Background:** the effects of the timing of CRRT initiation and the characteristics of the infectious process on the clinical outcomes in sepsis patients seem to be controversial. In this study, we tried to elucidate whether the timing of CRRT application, based on the interval between the start time of vasopressors infusion and CRRT initiation, was an independent predictor for mortality in critically ill patients with AKI.

Methods: We evaluated patients with AKI who were treated in ICU of Kosin University Gospel Hospital from January 1, 2010 to December 31, 2011. A total of 200 consecutive patients were included over a 48 month period. Predictors of all-cause death were examined using the Kaplan-Meier and Cox proportional hazards analyses in both treatment groups

Results: The main contributing factors of AKI were sepsis (38%) and cardiac dysfunction (40%). 28-day overall mortality rates in the early CRRT group were significantly lower than those in the late CRRT group ( $P = 0.001$ ). Furthermore, early CRRT treatment was independently associated with a lower mortality rate even after adjustment for age, sex, DM, and number of failed organ ( $P = 0.023$ ).

Conclusions: Early initiation of CRRT may be of benefit



#### 34. Immunomodulation with a selective cytopheretic device (SCD) improves myocardial contractility and renal sodium excretion in a canine model of congestive heart failure

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<sup>1</sup>Univ of Michigan, <sup>2</sup>Innovative BioTherapies, <sup>3</sup>CytoPherx, <sup>4</sup>Henry Ford Hospital

Immunomodulation with a selective cytopheretic device (SCD) improves myocardial contractility and renal sodium excretion in a canine model of congestive heart failure.

HD Humes 1,2,3; D Buffington1; A Westover1; HN Sabbah4

1Innovative BioTherapies; 2Univ of Michigan; 3CytoPherx; 4Henry Ford Hospital

Background: Cardiorenal syndrome (CRS), the most severe subset of patients with CHF, is characterized by diuretic resistance in volume overload and is a common problem faced by the critical care team. Current therapy is limited and new innovative approaches are needed. CHF is characterized by a proinflammatory state. The cytokines, TNF-alpha and IL-6, inhibit mitochondrial respiration and depress cardiac contractility (CC). Monocytes and tissue macrophages are sources of

systemic inflammation in CHF. Systemic monocyte levels correlate with poor outcome in CHF. The SCD, a novel biomimetic device, when placed in an extracorporeal circuit with regional citrate (c) anticoagulation has been shown to be an effective immunomodulatory device in acute multiorgan organ failure.

Method: To evaluate the acute effects of the SCD in a canine model of CHF, three groups of animals were evaluated during 4 hours of treatment: SCD-C, SCD-Heparin (H), and a sham control (S-C), n=2-5 in each group.

Results: Left ventricle (LV) ejection fraction (EF) increased substantially in the SCD-C group from  $34 \pm 2.3$  to  $48 \pm 3.7\%$  while SCD-H and S-C (n= 2-5) did not change. This effect was not due to a decline in systemic vascular resistance (SVR) which was similar in all groups. Ventriculograms demonstrated the SCD-C to convert viable but non-contracting myocardium to better contracting myocardium. The renal effects were also substantive. The fractional excretion (FE) Na nearly doubled in the SCD-C compared to SCD-H increasing from  $2.2 \pm 0.8$  to  $5.3 \pm 0.8\%$  and FE Urea went from  $59 \pm 3.1$  to  $81 \pm 11.3\%$ . No adverse events of arrhythmia or hypotension were observed during treatment. Isolated peripheral blood monocytes showed a decline in IL-6 and TNF-alpha secretion at end of treatment compared to baseline demonstrating a change in proinflammatory phenotype.

Conclusions: These results demonstrate that immunomodulation with the SCD improves left ventricular function and improves natriuresis. Removal of the cardio depressant effects of the chronic inflammatory state of CHF may be a new innovative approach to the management of CRS in critically ill patients.

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### **35. The Monitoring of Serum Neutrophil Gelatinase-associated Lipocalin Who Received CRRT due to AKI After Organophosphate Intoxication**

Joon Seok Oh<sup>1</sup>, Seong Min Kim<sup>1</sup>, Yong Hun Sin<sup>1</sup>, Joong Kyung Kim<sup>1</sup>

<sup>1</sup>*Bong-Seng Memorial Hospital*

Background: Predicting recovery of renal function for whom have acute kidney injury supported with renal replacement therapy is one of the top ten questions. Neutrophil gelatinase-associated lipocalin (NGAL), a 25-kDa protein is known as a potential tool for determination of renal replacement therapy initiation but it is not clear as a determination tool for termination. So we investigate the serum NGAL in patients received continuous renal replacement therapy(CRRT) due to acute kidney injury after organophosphate intoxication.

Methods: Ten patients undergoing CRRT after organophosphate intoxication were included in this study. The Serum NGAL levels of the subjects were measured on the start day of CRRT and the stop day of CRRT. The NGAL levels were measured using a research-based enzyme-linked immunosorbent assay with detection limit of 0–1,300 ng/mL. Data are presented as mean  $\pm$  SD for all data and wilcoxon signed ranks test was used.

Results: The average duration of CRRT was  $5.60 \pm 3.34$  days. The serum NGAL level of CRRT on the start day was  $717.70 \pm 508.79$  ng/mL, and that of CRRT on the stop day was  $687.70 \pm 482.49$  ng/mL. There was no statistically significant difference of the NGAL values between initiation and termination CRRT date.

Conclusion: It has shown that the recovery of AKI does not substantially influence plasma NGAL concentration. Therefore it may not need to be measured plasma NGAL levels as an indicator for persistent renal injury or renal recovery in patients with AKI after organophosphate intoxication.





### 36. Prospective Observational Study of Acute Injury Rates Post-Cardiothoracic Surgery

James A Tumlin<sup>1</sup>, Claude M Galphin<sup>2</sup>, Rick Andrews<sup>3</sup>

<sup>1</sup>University of Tennessee College Medicine, <sup>2</sup>Southeast Renal Research Institute, <sup>3</sup>Thrasos Corporation

Acute kidney injury (AKI) is a common complication of hospitalized patients that is associated with markedly increased morbidity and mortality. Acute kidney injury is a post-operative complication in 5 to 30% of patients undergoing cardiac vascular surgery (CVS). For patients progressing to dialysis in-hospital mortality has consistently ranged between 60-70%. Study Design: The proposed study is a prospective, multi-center, observational study of the rate of acute kidney injury (AKI) following cardiothoracic surgery in an at risk population with defined co-morbid risk factors.

Total Enrollment: 125 cardiothoracic patients undergoing coronary bypass with without valve replacement and additional risk factors for post-operative AKI.

Study Screening-Cardiothoracic Variables:

- a) "On-pump" CVS patients undergoing bypass or valve replacement aortic root repair
- b) Cardiomyopathy with left ventricular ejection fraction (EF) of < 40%
- c) "On-pump" cardiac bypass time exceeding 100 min
- d) "On-pump" cardiac bypass aortic cross clamp time exceeding 60 min
- f) Intra-operative hypotension defined as SBP < 70 mm Hg for > 5 minutes
- g) Patients with cardiac index < 2.5 L/min on two episodes during a single 24 hour period with or without the use of intravenous cardiac inotropes
- h) Any post-CVS patient requiring 2 or more Inotropes
- i) Any post-CVS patient requiring support with intra-aortic balloon pump

Study Patient Screening Parameters- Chronic Kidney Disease (CKD)

- a) All patients with serum creatinine (Cr) 1.2 > or < 2.1 mg/dl OR CKD stage III (estimated GFR 30 to 59 mL/min) determined by MDRD or Cockcroft Gault
- b) Exposure to iodinated contrast agents 48 hour prior to screening
- c) Patients with +2 proteinuria on pre-operative urinalysis

Primary Study Objective: To determine the incidence of AKIN criteria stage II in patients undergoing cardiothoracic surgery and pre-defined set of co-morbid risk factors.

Secondary Study Objective: To determine the percentage of patients with a defined set of co-morbid risk factors require renal replacement therapy or sustained CKD on post-operative Days 28, 60 and 90. Using these time points, we will determine the time to renal recovery and correlate that with risk groups POR-1, POR-2 and POR-3.

Summary: The observational study is the first to pre-operatively define a set of CVS risk factors and determine the true incidence of AKI in a defined patient population.

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### 37. Interobserver Reliability in Diagnosing Acute Kidney Injury Using AKIN Criteria

Akhoundi Abbasali<sup>1</sup>, Balwinder Singh<sup>1</sup>, Pablo Moreno Franco<sup>1</sup>, Vitaly Herasevich<sup>1</sup>, Guangxi Li<sup>1</sup>, John Lieske<sup>1</sup>, Ognjen Gajic<sup>1</sup>, Kianoush B Kashani<sup>1</sup>

<sup>1</sup>Mayo Clinic, Rochester, MN

Purpose: Acute kidney injury (AKI) is a common complication in intensive care units, affecting more than 35% of critically ill patients. Thus early detection is important for favorable outcomes. The preferred definition for AKI is based on the Acute Kidney Injury Network (AKIN) criteria. However the accuracy and reliability of the AKIN criteria determined by retrospective chart review has not been evaluated. Therefore, we conducted this study to assess the interobserver reliability in diagnosing AKI using AKIN criteria.

Methods: Two independent mutually masked physician investigators retrospectively reviewed electronic medical records including clinical notes, intake/output charts, and laboratory data of adult patients (≥ 18 yr ages) consecutively admitted to



the Mayo Clinic Rochester ICUs between 1/12/2010 to 2/28/2010. The diagnosis of AKI by AKIN criteria were determined based upon an increase in serum creatinine and decrease in urine output. Patients without research authorization, patients with end stage kidney disease on renal replacement therapy at admission, and those who were diagnosed with AKI before ICU admission were excluded from the final analysis. Interobserver agreement between the two reviewers was calculated using Cohen's weighted  $\kappa$ .

Results: Of 640 adult patients who met our inclusion criteria, 286 (44.7%) were females with a median age of 66 years (IQR 51-75); 570 (89%) were Caucasians. The median APACHE III score and SOFA scores were 61 (IQR 49-78) and 2 (IQR 4-6), respectively. Seventy one were prevalent AKI episodes, and 44 were end stage renal disease cases. The Interobserver agreement between the two reviewers for the diagnosis of AKI was excellent ( $\kappa = 0.965$ ; 95% confidence interval [CI] = 0.942 - 0.989).

Conclusions: We conclude that the interobserver agreement to retrospectively assess AKI by the AKIN criteria is excellent. These studies demonstrate that AKI detection by manual chart review is reproducible and suitable for clinical studies.

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### 38. Predictive Role of Fibroblast Growth Factor-23 in Continuous Veno-Venous Hemofiltration

Shilpa Sharma<sup>1</sup>, Marta Christova<sup>2</sup>, David Leaf<sup>1</sup>, Harald W Jueppner<sup>3</sup>, Sushrut S Waikar<sup>1</sup>

<sup>1</sup>Brigham & Women's Hospital, <sup>2</sup>Beth Israel Deaconess Medical Center, <sup>3</sup>Massachusetts General Hospital

#### Purpose of the study

Fibroblast Growth Factor (FGF)-23 is a bone derived regulator of phosphate homeostasis that is elevated in chronic kidney disease and associated with poor long term outcomes. Emerging evidence suggests FGF-23 levels are elevated in acute kidney injury (AKI) and may be associated with adverse clinical outcomes. By collecting corresponding effluent and plasma samples during multiple time points in the course of CVVH, we found FGF-23 is cleared during CVVH with a sieving coefficient of 0.27 ( $\pm 0.08$ ). We sought to measure and compare effluent FGF-23 levels at CVVH initiation between 1-yr survivors and non-survivors.

#### Methods

CVVH was applied using biocompatible polyether sulphone membranes (Hemofilter size:1.6 m2), pre-dilution mode using bicarbonate or citrate replacement solution at 1600-3000ml/hr.

C-terminal FGF-23 levels was measured in CVVH effluent samples collected using a partial effluent collection device that continuously sampled 1% of total effluent volume from 30 oligo-anuric patients with severe AKI.

#### Results

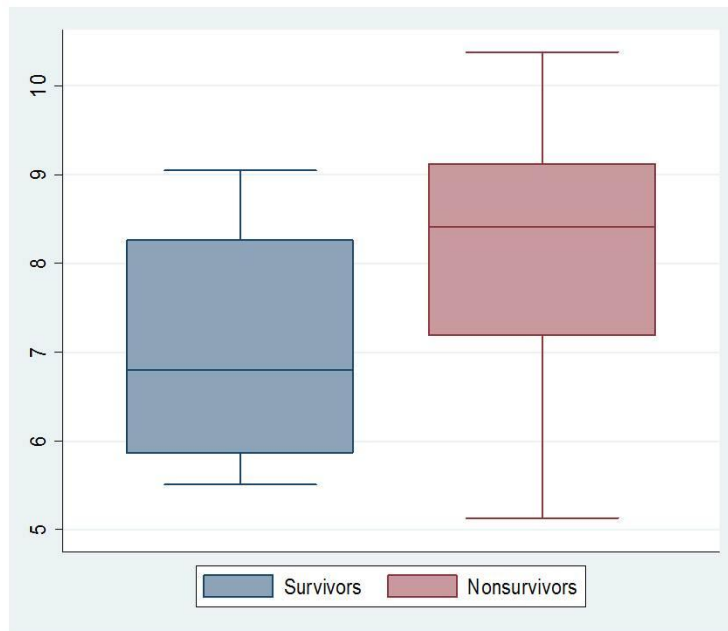
There was no statistical difference in baseline characteristics between survivors and non-survivors as shown in the table. Median FGF-23 in non-survivors was 4518.33 RU/ml (IQR: 1326.7 -9163.73) and survivors was 895.6 RU/ml (IQR: 354.3-3876.65). Median FGF-23 levels significantly lower in survivors compared to survivors at CVVH initiation ( $p=0.02$ ). Figure shows box plots of natural log transformed FGF-23 in survivors and non-survivors

#### Discussion

FGF-23 is a 26-kD protein with key role in maintenance of normophosphatemia. Emerging evidence suggests that FGF-23 may have direct pathogenic effects and causal role in the pathogenesis of LVH. We found that FGF-23 levels at CVVH initiation are significantly higher in non survivors as compared to survivors and that FGF-23 is cleared during CVVH. Our pilot studies suggest that FGF-23 could have a role as a biomarker of poor outcomes in severe AKI. Future studies will need to clarify FGF-23's role in AKI as a biomarker or mediator of disease outcomes and whether therapies aimed at reducing FGF-23 levels may be beneficial.

(table and figure on following page)

	Survivors	Non-Survivors	P-Value
Baseline Characteristics			
Age (years)	63.5 ( $\pm 12.2$ )	60.7 ( $\pm 10.6$ )	0.5
Gender (males, %)	67	70	
Weight (kg)	92.8 ( $\pm 18.8$ )	91.7 ( $\pm 20.3$ )	0.9
CKD (Defn: GFR<60) (%)	37	35	
Cause of AKI (ATN, %)	66	65	
CVVH Parameters			
Dose (ml/kg/hr)	21.15 ( $\pm 6$ )	23.6 ( $\pm 5.7$ )	0.1
Duration (days)	7.3 ( $\pm 3.9$ )	7.7 ( $\pm 5$ )	0.8
Laboratory			
Creatinine (mg/dl)	3.66 ( $\pm 1.4$ )	3.68 ( $\pm 1.2$ )	0.9
Phosphorus (mg/dl)	5.3 ( $\pm 1.8$ )	6.49 ( $\pm 1.7$ )	0.13



### 39. Peritoneal Dialysis Can Modulate the Urine Biomarker Profile in Children Who Undergo Complex Cardiac Surgery Using Cardiopulmonary Bypass Surgery

David Askenazi<sup>1</sup>, Rajesh H Koralkar<sup>1</sup>, Sahar Fatallah<sup>1</sup>, Santiago Borrassino<sup>2</sup>, Satish RamachandraRao<sup>3</sup>, William C Sasser<sup>2</sup>, Jeffrey A Alten<sup>2</sup>

<sup>1</sup>Pediatric Nephrology University of Alabama at Birmingham, <sup>2</sup>University of Alabama at Birmingham, Division of Pediatric Critical Care, <sup>3</sup>UC San Diego School of Medicine, Nephrology Division

Background: AKI is common in children who undergo cardiac surgery with cardiopulmonary bypass (CPB). The optimal timing of renal support therapy for children at risk for AKI and fluid overload (FO) is unknown. Many center use peritoneal dialysis (PD) shortly after CPB to prevent FO and reduce inflammation. Urine biomarkers can predict CPB-AKI but the

impact of PD on urine biomarker levels is unknown.

Objectives: 1) To compare concentrations of 8 urine AKI biomarkers between children with and without AKI. 2) To determine if PD alters urine AKI biomarkers compared to passive drain.

Design/Methods: Using a before and after prospective intervention design, we enrolled two groups of patients undergoing complex cardiac surgery with CPB (median age 8 days). Group 1 (drain; n= 16) was enrolled between January and June 2011, and received an abdominal catheter for passive drainage. Since June 2011, group 2 (PD; n=27) was started on active PD shortly after surgery, once hemodynamically stable (median 2.5 hrs after admission). PD was initiated using 1.5% Dianeal, 10 cc/kg dwell, dwell time 40 min, and hourly cycles. Eight urine biomarkers were analyzed at CICU admission (time 0) and 24 hours after CICU admission (time 1 day) and compared between AKI and no AKI subjects using Kruskal-wallis test. AKI was present if SCr rose  $\geq 0.3$  mg/dl from baseline in drain group or SCr  $\geq 0.2$  mg/dl in PD group. Baseline SCr value was determined by the lowest SCr 1 wk before or 1 wk after CPB surgery. Linear regression was performed to model the log of each biomarker to determine differences between a) PD vs. Drain groups, b) time 0 and 1, c) AKI, and d) the interaction of groups X time.

Results: At CICU admission, NGAL was higher in AKI compared to no AKI subjects ( $p < 0.04$ ); Uromodulin (UMOD) trended higher in AKI subjects ( $p < 0.07$ ). At 24 hours of CICU admission, NGAL trended higher in AKI vs. no AKI ( $p < 0.07$ ). After controlling for AKI status, the log concentrations of urine Cystatin C, osteopontin, uromodulin, and epithelial growth factor differed significantly for the interaction of time X group ( $p < 0.02$ ).

Conclusions: In this small cohort of children, urine NGAL was associated with CPB associated AKI. Urine AKI biomarker levels differ over time in those who receive PD vs. passive drain. Studies to delineate whether this is due to enhanced clearance, alterations of renal perfusion between PD vs. Drain subjects, or systemic response to active PD are needed.

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## RRT TECHNIQUE CHARACTERISTICS

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### 40. The Role of Plasmapheresis in Organophosphate Poisoning with Two Pediatric Patients Who Do Not Respond to Standard Treatment

Dinçer Yıldızdas<sup>1</sup>, Ufuk Yükselmiş<sup>1</sup>, Levent Yılmaz<sup>1</sup>, Yusuf Sari<sup>1</sup>

<sup>1</sup>Çukurova University, Pediatric Intensive Care Unit, Turkey

Aim: To assess the impact of plasmapheresis used in the management of two pediatric cases with organophosphate poisoning.

Patients : Two patients with severe organophosphate poisoning who do not respond to standard treatment.

Treatments: The treatment of signs and symptoms, supportive treatment, Atropine, Pralidoxim, Plasmapheresis.

Case Presentation: Two sisters aged five and seven who had signs of miosis, abdominal pain, vomiting, confusion, respiratory failure after their mother washed their hair with organophosphates and then the girls became sick and they were brought to the pediatric emergency department. They were taken to pediatric intensive care unit after the detection of Pseudocholinesterase levels 398 U / L and 428 U / L. The patients were given atropine infusion (0.08 mg / kg / hr) and five-minute intervals atropine 0.05 mg / kg / dose. For three times, pralidoxim loading and pralidoxim infusion were applied. Because of the worsening of clinical signs, patients were intubated and connected to mechanical ventilation. However, despite standard treatment, clinical symptoms did not improve and there was no change in plasma pseudocholinesterase levels. Therefore, plasmapheresis was done on three consecutive days. Consequently, the clinical signs improved, and there was no need for mechanical ventilation. Patients were discharged on the sixteenth day after their admission to the hospital.

Conclusion: In organophosphate poisoning, plasmapheresis can be considered as an option for the patients who do not respond to atropine and pralidoxim treatment.

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#### 41. A Comparison of Estimated Creatinine Clearance and Measured Glomerular Filtration Rate (Tc99mDTPACclearance) in Indians

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<sup>1</sup>Rajeev Gandhi College, Chopal, India, <sup>2</sup>Jawahar Lal Nehru Cancer Hospital & Research Centre, Bhopal

##### Abstract

**Background:** The aim of this study was to compare measured glomerular filtration rate (GFR) with estimates of GFR derived from various estimated creatinine clearance methods of Jelliffe, Cockcroft and Gault, and 4MDRD equations in Indian population.

**Methods:** We enrolled 80 patients in the study. GFR was determined by Tc99mDTPA clearance. Height, body weight and serum creatinine were measured, and GFR and creatinine clearance (CrCl) estimates calculated by various equations. Spearman's correlation was used to assess relationships between measured GFR (Tc99mDTPA clearance) and estimated clearances using the three formulae. Difference between the measured GFR and estimated clearances compared with measured GFR were examined to determine whether prediction error was independent from measurement magnitude. Analyses of differences were used to determine bias and precision. Bias was assessed by mean percentage error (MPE), calculated as the percentage difference between the estimated clearances for each formula and measured GFR. A positive bias indicates overestimation of GFR, and a negative bias indicates underestimation. Relationships were also assessed by gender and varying levels of renal function: GFR <60 ml / min, and GFR >60 ml / min.

**Results :** The mean measured GFR was 77.2 ml / min (range 17 to 152 ml / min). The mean bias (mean percentage error) was -4.9, -10.3 and -1.57% respectively for the, Jelliffe, Cockcroft and Gault, and 4MDRD formulas, respectively. The 4 MDRD formula overestimates the GFR in patients having GFR less than 60ml / min, whereas it underestimates for GFR more than 60ml / min.

**Conclusions:** 4 MDRD equation seems to be most efficient in estimating GFR in Indian population.

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#### 42. Citrate Toxicity During CRRT After Massive Transfusion

Carl Walther<sup>1</sup>, Amber S Podoll<sup>1</sup>, Kevin W Finkel<sup>1</sup>

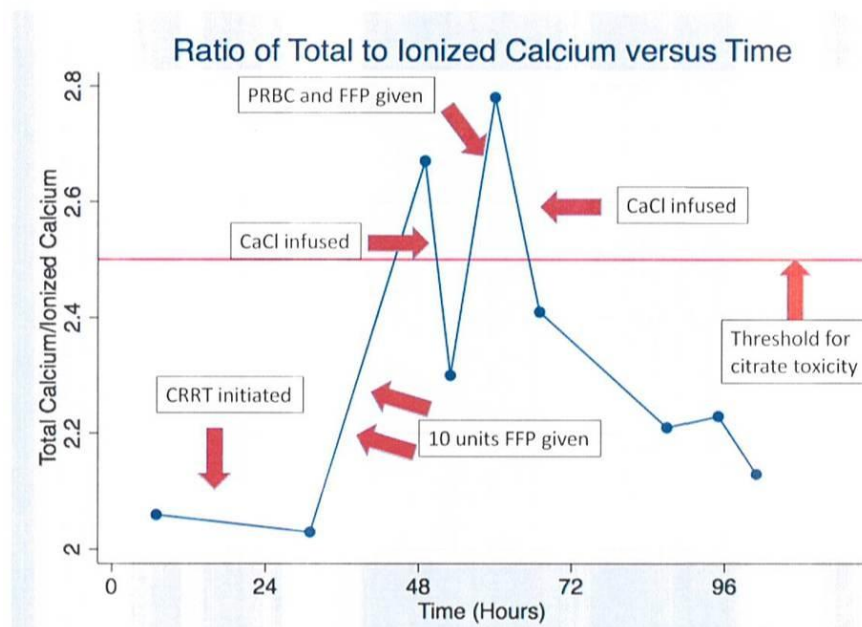
<sup>1</sup>UTHealth Science Center at Houston

Regional citrate anticoagulation (RCA) is commonly used in continuous renal replacement therapy (CRRT). Citrate, by chelating calcium (Ca), is also used to inhibit coagulation during storage of blood products. The normal liver rapidly metabolizes citrate to bicarbonate and releases bound Ca, but liver dysfunction reduces this ability and predisposes to citrate toxicity during CRRT with RCA. Citrate toxicity is detected by an elevation in the total to ionized Ca ratio (TCa/iCa).

A 51 year-old woman with cirrhosis due to chronic hepatitis B (HBV) was admitted to the intensive care unit for acute liver failure, thought to be due to rapid HBV replication after she stopped taking antiviral medication because of side-effects. During the next two weeks she developed encephalopathy, coagulopathy, lactic acidosis, and oliguric acute kidney injury. Continuous veno-venous hemofiltration (CVVH) was started without anticoagulation. Because of a gastrointestinal hemorrhage, the patient received 10 units (2.6L) of fresh frozen plasma (FFP), and one unit of packed red blood cells (PRBC). She developed hypotension and was found to have an iCa level of 0.88 mmol/L, a TCa level of 9.4 mg/dL, and an elevated TCa/ iCa ratio of 2.67. This ratio was significantly higher than prior to the administration blood products and is above the threshold value for citrate toxicity of 2.5. Two grams (14 mmol) of calcium chloride (CaCl<sub>2</sub>) were given, and an infusion of CaCl<sub>2</sub> at 1 mmol/hr was started. After these interventions iCa normalized, with reduction of the TCa/ iCa ratio below 2.5. The CaCl<sub>2</sub> drip was stopped. The following day she was given 4 units PRBC and 4 units FFP, developed low iCa and elevated TCa/iCa ratio, and was re-treated with another bolus and infusion of CaCl<sub>2</sub> (Figure 1). The bleeding eventually

resolved without intervention. With no further large-volume transfusions, the calcium derangements did not recur. CVVH was continued, but the patient deteriorated and subsequently was transitioned to comfort care.

Citrate toxicity is not uncommon in patients with liver failure undergoing CRRT with RCA and is monitored by measuring the TCa/iCa ratio. However, as this case illustrates, liver failure patients who receive massive amount of blood products should equally be monitored for the development of citrate toxicity.



### 43. Rebound Alkalosis Using RCA in Liver Failure

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<sup>1</sup>UTHealth Science Center at Houston

Regional citrate anticoagulation (RCA) is an effective form of anticoagulation for continuous renal replacement therapy (CRRT). By chelating calcium, RCA inhibits the coagulation cascade within the extracorporeal circuit. While citrate is rapidly metabolized to bicarbonate by the normal liver releasing bound calcium, in the presence of liver failure unmetabolized citrate accumulates and citrate toxicity is detected by an increased total to ionized calcium ratio (TCa/iCa). We report a patient with acute liver and renal failure treated with CRRT and RCA who developed delayed life-threatening metabolic alkalosis after liver recovery.

A 32 year old woman presented to the emergency room in her 26th week of pregnancy with complaints of abdominal pain. She was noted to be confused and jaundiced with evidence of acute hepatic and kidney failure attributed to acetaminophen intoxication. She was treated with single pass albumin dialysis (SPAD) for 48-hours and then transitioned to CRRT with RCA (28 mM/hr sodium citrate). After two days the iCa level was low (0.93 mM/L) and the TCa/iCa ratio was elevated (2.7) consistent with citrate accumulation and toxicity. CRRT was immediately held and intermittent hemodialysis was initiated. The following day the iCa increased and was accompanied by recovery from acute liver failure manifested by improved bilirubin and transaminase levels and coagulation parameters. Over the next 48-hours the patient developed worsening metabolic alkalosis eventually reaching a bicarbonate level of 40 mM/L and an arterial pH of 7.7. The patient then experienced a tonic-clonic seizure attributed to alkalosis-induced hypocalcemia. Hydrochloric acid (HCl) and calcium were administered by continuous infusion with eventual improvement in the alkalosis. However the patient's condition continued to deteriorate and it was decided to withdraw care.

Although the use of RCA with CRRT is effective and generally safe, in patients with liver failure citrate can accumulate and is detected by an increased TCa/iCa ratio. Most reports on citrate toxicity focus on the management of the ionized hypocalcemia and acidosis due to the lack of citrate metabolism. Here, we report an unusual case of rebound alkalosis in a patient with citrate accumulation after recovery of liver function. It demonstrates that the use of RCA in the presence of liver failure is complex and requires extreme diligence when applied.

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#### **44. Importance of using Citrate Anticoagulation for CVVHDF in a Patient with Hemolytic Uremic Syndrome (HUS)**

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A 5 year-old patient, was admitted to the hospital because of three day of diarrhea and respiratory distress, accompanied by intractable vomiting. A coproscopic test indicated amoebic diarrhea, later he was sent home with metronidazole and oral electrolyte solution. Without improvement, two days later returns to pediatric ER, in that moment having more diarrhea episodes and looking very dehydrated. Laboratory exams were taken, hemogram reports 7.5 hemoglobin level, creatinine 2 mg/dl and urea nitrogen 56, LDH of 3147, platelets 44000. Diagnosis was performed, diarrheic disease with high grade of dehydration, acute renal failure and suspected HUS.

Patient was admitted to PICU, where peritoneal dialysis was started for the next 5 days, without clinical improvement therefore decides initiated continuous renal replacement therapy in the form of continuous venovenous hemodiafiltration, by this moment the patient was hemodynamic compromised looking lethargic, pale, drowsiness and septic. Hemoglobin 8, hematocrit 22, platelets 37000, creatinine 6.5 BUN 6.5; Anuric, positive water balance with 988ml, arterial blood gases reported pH 7.3, PCO<sub>2</sub>: 35, PO<sub>2</sub> 40, HCO<sub>3</sub>: 17.2, EB: -7.8 ( Hypoxaemic metabolic acidosis). CRRT was programmed in mode: continuous venovenous hemodiafiltration, pump flow: 80 to 160 ml / min (5-10 ml / kg / min); Ultrafiltration: 228 cc / h. Using Citrate anticoagulation, it was place 1.5 times the pump flow bone. 10% Calcium gluconate infusion: 15 ml / h. Dialysate Dose: 60 cc / kg / h distributed as follows: predilution: 480 cc / h postdilution: 480 cc / h. Control testing was due every 2-4hours. During CRRT, using citrate anticoagulation the length and half-life of the filter was 7 days, just two filters were use with no complications. Patient evolution was satisfactory. The patient recovered normal renal function, and output was given from pediatric intensive care unit 20 days later.

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#### **45. An Alternate Technique for Circuit Blood Priming in Patients Requiring Multiple Extracorporeal Therapies**

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The safety and efficiency of delivering extracorporeal therapies, such as Continuous Renal Replacement Therapy (CRRT) and Therapeutic Plasma Exchange (TPE) in the pediatric and neonatal population, has improved significantly with the availability of technologically advanced machines. However, available circuits present a challenge for the smallest patient, due to the extracorporeal volume comprising a significant portion of the patient's estimated blood volume resulting in the need for blood priming the circuit. This issue is magnified when the patient requires multiple extracorporeal therapies and/ or treatments. In an effort to decrease the exposure to multiple blood products for patients requiring several extracorporeal circuits and treatment, we describe a technique using one machine circuit to prime the other machine circuit. Special considerations for the patient and/or circuit are the hematocrit, and differences in circuit volume. The procedure consists of disconnecting the current extracorporeal access line from the patient, connecting it to saline solution. Using a hemodialysis recirculation connector, the return line of the current extracorporeal circuit was connected to the new circuit access. The blood flow rate was set at 50 mL/minute and both machines were started simultaneously. Once the new extracorporeal circuit



was primed with blood, the new circuit was disconnected from the old circuit, and connected to the patient access. This procedure was trialed for a 9.8 kg patient diagnosed with hemophagocytic lymphohistiocytosis and associated multiorgan failure, receiving both CRRT and TPE. Each procedure required blood primed circuits. CRRT was performed with the Prismaflex™, using the M60 filter set. TPE was performed with the Cobe Spectra™, using the exchange set. Patient's vital signs remained unchanged during the circuit exchange procedure; specifically, the Mean Arterial Pressure which ranged between 78-84 mmHG. Although similar techniques have been described, the previous procedures utilized identical machines via membrane to membrane. The current procedure was applied using different machines and circuit sizes, specifically membrane and centrifugal circuits. The procedure decreases the patient exposure to blood products and costs associated with dilutional product preparation. Additionally, this procedure eliminates patient wait times, decreases membrane reactions, and improves efficiencies.

#### 46. Novel Approach to Hemodialysis Access Using Two Single Lumen Catheters in Infants With Cardiac Disease

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**Background:** Acute kidney injury (AKI) frequently occurs in neonates and infants after cardiopulmonary bypass (CPB) and many require renal replacement therapy (RRT). Peritoneal dialysis is the RRT modality of choice in neonates with AKI after CPB, but hemodialysis may be necessary if PD is ineffective or contraindicated. Vascular access is challenging due to small central vein size or thrombosis that may preclude placement. In addition, the risk of malfunction or morbidity associated with standard dialysis catheters may be excessive in neonates with congenital heart disease. We report our approach to vascular access for hemodialysis in four small patients with AKI after CPB.

**Methods:** Retrospective review of five patients with fluid overload and AKI after cardiac surgery that received hemodialysis after ineffective PD. In all cases, ultrasound guidance was used to place 4 or 5 French hemostasis valve introducer catheters into separate veins for dialysis machine access and return. Continuous hemodiafiltration was initiated via Gambro Prismaflex machine with heparin anticoagulation.

**Results:** The catheters provided excellent blood flow (C-clamp required on all return lines as dialysis machine detected low pressures). All patients achieved excellent normalization of metabolic derangement and fluid removal. There was no dialysis discontinuation due to mechanical problems.

**Conclusion:** Vascular access via two small single lumen catheters in separate veins enables consistent and effective dialysis and ultrafiltration in neonates with small vessel size and high risk of vascular thrombosis and obstruction. This is an alternative technique to traditional larger double lumen catheters that are often ineffective and associated with morbidity in this population.

Patient	Age and Gender	Weight	CHD	Surgery	PD Complications
1	4days, F	2.5 kg	HLHS	Sano-Norwood	Pleuro-peritoneal communication
2	7days, M	3.4 kg	DILV, LTGA, CoA	DKS, BT shunt ECMO Berlin Heart	Omental herniation
3	1year, F	8.5 kg	D-TGA, VSD, Cardiomyopathy	ECMO Berlin Heart	Peritonitis
4	7days, F	3.7 kg	Aortic arch hypoplasia, ASD, Scimitar Syndrome	Arch Augmentation, ASD closure ECMO	Pleuro-peritoneal communication
5	15days, F	3.1 kg	D-TGA, VSD	ASO, VSD Closure -ECMO	Mechanical Obstruction

## 47. High Dose CVVHD Immediately After Liver-Kidney Transplant in Primary Hyperoxaluria Type 1

Helen P Pizzo<sup>1</sup>, Julia W Tzeng<sup>1</sup>, Robert B Ettenger<sup>1</sup>, Joshua J Zaritsky<sup>1</sup>

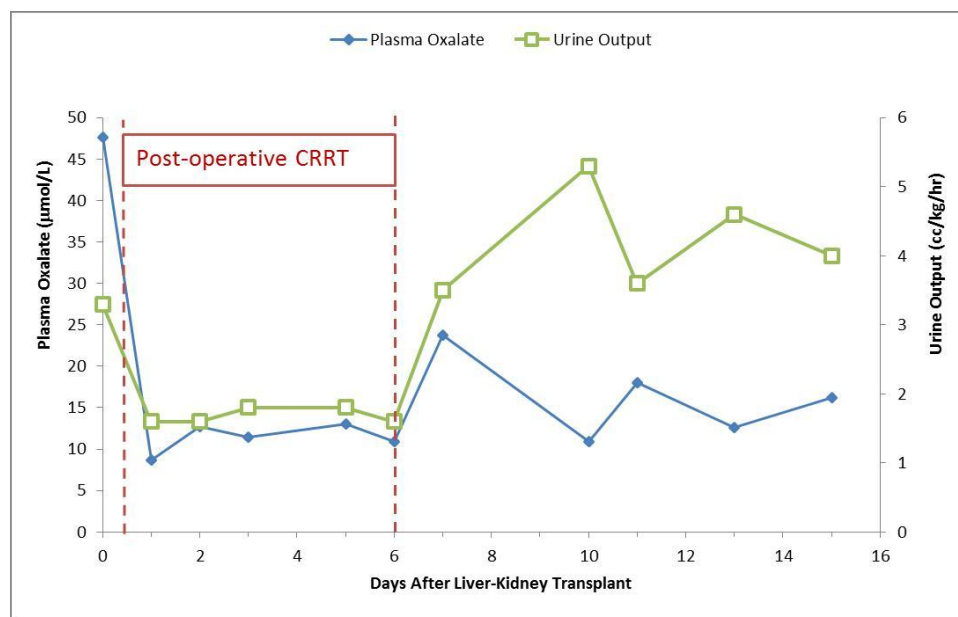
<sup>1</sup>David Geffen School of Medicine at UCLA

**Purpose:** A patient with primary hyperoxaluria type 1 (PH1) faces a high oxalate burden after a liver-kidney transplant (Tx) placing the renal allograft at risk for calcinosis, decreased function, and even Tx loss if delayed allograft function (DGF) limits urine output in the immediate post-operative period. Thus we evaluated the utility of high dose continuous veno-venous hemodialysis (CVVHD) as an ancillary method to decrease plasma oxalate (Pox) in the setting of DGF.

**Methods:** The patient was a twenty-month-old female with biopsy proven PH1 (AGXT mutation c.33dupC) weighing 11 kg who had been on dialysis for seventeen months prior to her en-bloc liver-kidney Tx. Intra-operatively, there were 60 minutes of warm ischemia resulting in low urine output and DGF. Post-operatively, high dose CVVHD was initiated with the NxStage System One® machine to maximize oxalate clearance in the setting of DGF with a Qb of 90 ml/min and Qd (Prismasate® 4K/2.5Ca) of 2000 mL/hr without any ultrafiltration or anticoagulation. This provided a calculated small molecule clearance of approximately 7000 ml/hr/1.73m<sup>2</sup>, 3.5 times the standard pediatric dose of 2000 ml/hr/1.73m<sup>2</sup>. The patient remained on CVVHD until her urine output improved on post-operative day six.

**Results:** Despite the decreased urine output for several post-operative days, Pox was maintained below 15 mcmol/L using CVVHD with an estimated oxalate clearance of 2000 ml/hr (1176 ml/week/1.73m<sup>2</sup>) (see Figure). Such oxalate levels are well below the critical Pox saturation point of 50 mcmol/L. Upon discontinuation of CVVHD there was a slight rebound in Pox, however, the level was still below the solubility threshold at 23.7 mcmol/L.

**Conclusion:** High dose CVVHD is an effective technique to minimize Pox in the post-Tx period for patients with PH1. The use of high dose CVVHD should be strongly considered in patients at risk for DGF, as low urine output leads to decreased oxalate clearance and puts the Tx at great risk.



#### 48. Observational Study: Utilisation of Citrate vs Heparin Anticoagulation for Continuous Renal Replacement Therapy in Intensive Care Unit May Reduce Patients Need for Blood Transfusion

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<sup>1</sup>West Suffolk Hospital

Citrate is an anticoagulant agent which has shown promise with favourable efficacy and safety profiles for use during continuous renal replacement therapy (CRRT). These benefits have been well reported in the literature, however there has only been very limited number of studies comparing citrate to heparin, which is more commonly used in CRRT. As one of first intensive care units within East Anglia (UK) to use citrate in place of heparin, we have conducted a study to compare the transfusion frequency and volume associated with using these agents.

##### Methods:

We carried out a retrospective observational study to compare outcomes related to the use of heparin and citrate treatment protocols. The study population comprised the last 40 consecutive patients with acute kidney injury (AKI) requiring CRRT for more than 24 hours who received heparin or citrate. We excluded patients with active bleeding, pre-existing coagulopathy, previously known end stage renal failure and all surgical patients in our study. The ITU electronic records system (Metavision) was reviewed for patient demographics, cause of acute kidney injury, mean haemoglobin levels, transfusion frequency, transfusion volume and final outcome.

##### Results:

80 individual patients were selected based on the inclusion and exclusion criteria. There were 40 patients in each of the citrate and heparin treatment arms. Patient demographics are presented in the Table 1. There was no significant difference in the APACHE score, mean age of patients or mean duration of CRRT in both groups. Sepsis was the most commonly recorded cause of AKI (35 patients) followed by cardiac failure/arrest and hypovolaemia.

Significantly more packed red blood cells were transfused in the heparin group as compared to the citrate group (62 vs. 19,  $p=0.0059$ ) with 53.5% of all patients requiring a transfusion versus only 22.5% in the citrate group. However, the mean haemoglobin for both groups was not significantly different (9.7 vs. 10.0,  $p=0.2925$ ). In terms of final outcomes, there was no significant difference in mortality rates between both treatment groups (25% vs. 32.5%,  $p=0.6219$ ).

##### Conclusion:

This study shows that citrate as a regional anticoagulant agent demonstrated benefits over heparin in CCRT with respect to the need for transfusion, and total number of units transfused.

	Heparin Group	Citrate Group
APACHE Score	23.8	23.5
Mean Age (years)	65.73	67.53
Male: Female Ratio	22.18	24.16

#### 49. Retrospective Monocentric Analysis And Proposal Of A Flow-Chart to Avoid Circuit Clotting In Prolonged Intermittent Renal Replacement Therapy (PIRRT)

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<sup>1</sup>Nephrology, Dialysis and Kidney Transplantation Unit, University of Turin, Italy, <sup>2</sup>Nephrology and Dialysis Unit, Cuneo Hospital, Italy

Background and aim of the study: Premature circuit clotting is a key problem in AKI patients undergoing CRRT. PIRRT represents a dialysis modality combining the detoxification and hemodynamic stability of CRRT with the advantage of

conventional intermittent dialysis. However, the rate of circuit clotting in PIRRT is still high, leading to dialysis down-time. The aim of this study was to analyze the rate of coagulation during PIRRT in our centre and to elaborate a flow-chart to avoid circuit clotting and down-time.

Methods: We analyzed clotting episodes in all PIRRT performed in the period 2011-2012 (256 AKI patients, 1318 PIRRT sessions, 0.6-1.8 m<sup>2</sup> polysulphone membrane, duration of 10-12 hr, blood flow 200-250 ml/min, prescribed dose 25-30 ml/Kg/hr, predilution 30-40%). Statistical analysis was performed using the Hemer-Lemeshow test.

Results: Patients characteristics were: 68.4% males; age 66.5±6.1 yrs; serum creatinine at the start of PIRRT 4.28±0.84 mg/dl. Septic patients were 72/256 (28.1%). Circuit clotting was observed as follows: 70-100 % clotting in 6.5% of cases, 50-70% in 5.8%, 30-50% in 7.3%, 10-30% in 23.4%, <10% in 57%. The majority of clotting episodes were observed in the same individuals, in particular in septic patients with low levels of ATIII due to consumption. On this basis, we elaborated a flow-chart to avoid circuit clotting in PIRRT: 1) assessment of catheter and optimization of blood flow; 2) increasing predilution to 60-70% preserving an adequate transmembrane pressure; 3) decreasing PIRRT duration to 6-8 hours without compromising hemodynamic stability; 4) optimization of heparin dose (500-1000U/hr) and correction of ATIII levels > 80% without bleeding risk; 5) use of heparin-coated filters; 6) telemonitoring system to control intradialytic parameters; 7) use of alternative types of systemic anticoagulation (citrate).

Conclusions: Our retrospective study showed that: 1) the majority of PIRRT with low dose heparin (250-500U/hr) and 30-40% predilution occurred without clotting; 2) low ATIII levels exposed to an increased coagulative risk, in particular in septic patients; 3) clotting episodes occurred in the same patients leading to down-time; 4) reduction of dialysis duration, use of heparin-coated filters and telemonitoring system allowed an increased circuit life-span; 5) when all these strategies failed, regional citrate anticoagulation may be useful in PIRRT to avoid frequent and premature circuit clotting.

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## RRT APPLICATIONS AND TARGETED INTERVENTION

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### 50. Liposyn Use Precluding Renal Replacement Therapy

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<sup>1</sup>University of Mississippi

Intravenous lipid emulsion therapy is showing promise in reversal of drug induced cardiac toxicity. The evidence is currently based on animal studies and human case reports. Protocols exist for the administration of lipid emulsion in the setting of local anesthetic toxicity, though no optimal regimen has been established for treatment of acute non-local anesthetic poisonings. We present a case of an intentional overdose treated with intralipid therapy which resulted in lipemia and precluded renal replacement therapy.

A 26 y/o male presented after an intentional overdose of amlodipine, metoprolol, and lisinopril with hypotension refractory to IV fluids, calcium IV, glucagon and vasopressors. Intralipid therapy was started with an initial bolus of 120 mL, was then repeated after a minimal response. Continuous IV infusion at 0.25mg/kg/min was then planned for 4-6 hrs or until clinical improvement.

Approximately 5 hrs after admission, the patient was bradycardic, hypoxic and quickly deteriorated into PEA and respiratory failure. Labs at this time revealed renal failure with hyperkalemia and severe acidosis. Plans were made for emergent hemodialysis and during placement of HD catheter, thick lipemic appearing blood was noted. Intralipid therapy was stopped after a total of 5 hrs of continuous infusion (6.24 L total vol).

CRRT was attempted using Prismaflex and a HF 1400 dialyzer was used to prevent bradykinin release reaction given his ACE inhibitor ingestion. Within 1 hour of initiation, increased blood viscosity secondary to lipemia caused increased transmembrane pressures and clotting of the filter. A PD catheter was placed in attempts to bridge to CRRT with PD. Meanwhile plasmapheresis was started to improve the lipemia and the chance of successful CRRT. During plasmapheresis, the patient deteriorated hemodynamically despite intermittent boluses of epinephrine and maximum doses of 3 vasopressors. After 1.5 hrs of plasmapheresis, the patient's family decided to withdraw care and the patient died shortly thereafter.

The proposed mechanism of action for intralipid therapy is that it creates an expanded intravascular lipid phase that drives the

offending drug from target tissues into the newly formed lipid reservoir. There are many cases reporting success in reversing cardiac toxicity with the use of this therapy. However, the potential adverse events are less well known. This case highlights the complications of combining intralipid therapy with CRRT.

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## 51. Safety and Efficacy of Regional Citrate Anticoagulation in Sustained Low Efficiency Dialysis

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**Purpose:** To evaluate the safety and efficacy of regional citrate anticoagulation in sustained low efficiency dialysis (SLED). **Method:** We prospectively analyzed 45 patients of acute kidney injury (AKI) or end stage renal disease (ESRD) in nephrology division, West China Hospital, Sichuan University from August 2011 to September 2012. All the patients received SLED treatment by Fresenius4008sARrTplus dialyzer through either femoral or internal jugular venous catheter, with each session of SLED treatment lasting for 8 hours. We pumped in 4% tri-sodium citrate solution through the arterial line at 130ml/h and 10% calcium gluconate through the venous line at 40ml/h. The blood flow was 150ml/min while the calcium-free dialysate was delivered at 200ml/min. We recorded systemic citrate concentration, peripheral and post filter ionized calcium level at 0h, 2h and 5h respectively.

**Result :** 45 patients underwent 162 sessions of SLED. 2 sessions were discontinued for III° filter coagulation, while the rest 160 SLED sessions (98.8%) were all successfully performed. The systemic citrate concentration at 0h was  $0.14 \pm 0.06$  mmol/L, Although slightly increased, the systemic citrate concentrations at 2h and 5h were of no statistical difference ( $P > 0.05$ ), and post filter citrate concentrations at 2h, 5h were  $1.08 \pm 0.12$  mmol/L and  $1.11 \pm 0.17$  mmol/L. The 0h, 2h, 5h peripheral blood ionized calcium levels were  $1.04 \pm 0.13$  mmol/L,  $1.07 \pm 0.23$  mmol/L and  $1.04 \pm 0.24$  mmol/L respectively, with no significant difference ( $P > 0.05$ ), and post filter ionized calcium were recorded as  $0.31 \pm 0.04$  mmol/L (2h) and  $0.29 \pm 0.03$  mmol/L (5h). The trans-membrane pressure at 2h was  $104.5 \pm 17.8$  mmHg, and at 5h the value was  $104.5 \pm 17.8$  mmHg, however the increase was not statistically significant ( $P > 0.05$ ). At 5h, Prothrombin Time (PT) and Activated Partial Thrombin Time (APTT) were identified to be similar to those before SLED. During the treatments, no bleeding complication, thrombocytopenia, cardiac arrhythmia, hypernatremia, metabolic alkalosis or hypotension was observed. **Conclusion:** SLED under regional citrate anticoagulation is safe and effective. Citrate achieves satisfying regional anticoagulation effect without interfering systemic clotting function, thus provides a new option for SLED.

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## 52. Different Renal Replacement Therapy Modalities in Acute Kidney Injury Following Multiple Wasp Stings: 15 years of local experience

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**Objective** To investigate the effect of different modalities of renal replacement therapy (RRT) on acute kidney injury (AKI) following multiple wasp stings.

**Methods** 103 patients with multiple wasp stings injuries during 1997-2011 were retrospectively analyzed, in which 87 patients (84.5%) suffered AKI and 60 patients (68.9%) complicated with multiple organs dysfunction syndrome (MODS). In the 87 AKI patients, 81 patients (93.1%, APACHE II Scores:  $16.85 \pm 2.78$ ) received three different modalities of RRT: (1) CVVH group: Patients were treated with continuous veno-venous hemofiltration (CVVH) for at least 48h, and then turned to intermittent hemodialysis (IHD) when the condition of patients came to stable. (2) CVVH+PE group: Besides of the same RRT therapies as CVVH group received, patients were treated with plasma exchange (PE) twice on Day 1 and Day 2. (3) IHD group: Patients received IHD treatment three times per week.

**Results** 75 patients were followed up and 7 of them (9.3%) died. There was no difference in mortality rate between CVVH

group, CVVH+PE group and IHD group (8.0%, 7.1%, and 11.1% respectively,  $p>0.05$ ). All the survival patients in CVVH group and CVVH+PE group got complete recovery of kidney function. However, 8 patients in IHD group developed into chronic kidney disease (CKD), in which 2 patients developed to end stage of renal disease (ESRD). Besides, the recovery time of kidney function was obviously shorter in CVVH and CVVH+PE groups than IHD group ( $31.9\pm 8.5$ d,  $28.6\pm 9.4$ d, and  $41.6\pm 8.1$ d, respectively,  $p<0.05$ ). In the early stage, the serum bilirubin, creatine kinase, and myoglobin decreased faster in CVVH group and CVVH+PE group than IHD group ( $P<0.05$ ).

**Conclusion** We firstly reported the effectiveness of different RRT modalities in patients with severe AKI following multiple wasp stings. There was no significant difference in mortality between IHD, CVVH and CVVH+PE groups. However, CVVH could improve the renal outcome compared with IHD, especially combined with PE.



**Table 1. Primary kidney outcomes of patients in different groups**

Groups	Complete recovery <sup>*</sup>	CKD	ESRD	Death	Mortality rate <sup>#</sup>
IHD (n=36)	24	8	2	4	11.1%
CVVH (n=25)	23	0	0	2	8.0%
CVVH+PE (n=14)	13	0	0	1	7.1%

<sup>\*</sup>Comparison among groups in complete recovery rate: by Fisher's exact probabilities ( $P=0.02$ )

<sup>#</sup> Comparison among groups in mortality rate: by Fisher's exact probabilities ( $P=0.9$ )

**Table 2. Comparison of recovery time of kidney function**

	IHD (n=36)	CVVH (n=25)	CVVH+PE (n=14)	P value
Time of requiring RRT (d)	$22.6\pm 7.0$ <sup>*#</sup>	$14.4\pm 7.2$ <sup>*</sup>	$13.7\pm 8.3$ <sup>#</sup>	<0.001
Recovery of kidney function (d)	$41.6\pm 8.1$ <sup>*#</sup>	$31.9\pm 8.5$ <sup>*</sup>	$28.6\pm 9.4$ <sup>#</sup>	<0.001

Comparison among groups by ANOVA

Comparison between every two groups by Scheffe test (<sup>\*</sup> and <sup>#</sup>: there was significant difference between two groups)

### 53. Continuous Renal Replacement Therapy Combined With Endotoxins Removal In Septic Patients: A Pilot Study

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<sup>1</sup>San Camillo Forlanini, Rome, <sup>2</sup>European Hospital, Rome

**AIM:** we tested a recently developed CRRT membrane having enhanced adsorption capability on endotoxins (Oxiris, Gambro Hosal). This membrane is a AN69 based membrane, surface treated with a polyethyleneimine (PEI) and grafted with heparin (3000 UI/m ) to perform a combined treatment of CRRT and selective adsorption of endotoxins and cytokines in patients with acute kidney injury caused by severe sepsis or septic shock.

**MATERIALS AND METHODS:** we used the Oxiris membrane in CVVHDF with prescribed effluent dose of 40 ml/kg/h (40% diffusive and 60% convective) with Prismaflex on 34 patients with AKI having severe sepsis (n=23) or septic shock (n=11) from gram negative (n=28) and positive bacterial (n=6) infection after cardiac surgery. Different anticoagulation strategies (heparin, citrate, no anticoagulation) were applied during the treatments.



RESULTS: 34 patients (Age =65±10 y, Weight = 74±13 Kg, 8F/26M) received CRRT with use of 1.5±0.8 Oxiris sets per patient for average treatment time of 79±25 hours. Relevant improvements in terms of haemodynamic stability and renal function were found comparing before and after Oxiris treatment. In particular, an increase of mean arterial pressure and urine output combined with decrease of SOFA scores and norepinephrine dose were found (see table 1). These results were associated to a relevant decrease of inflammatory markers such as procalcitonin (PCT) and interleukin 6 (IL6) that decrease from 374±501 to 46±57 (p<0.01) ng/ml and from 76±89 to 12±15 (p<0.01) pg/ml respectively. Mortality rate at 28 days of 23% (10/34) and a good renal function recovery (19/23 patients + 1 ESRD) were found.

CONCLUSION: In our experience, the use of this new filter was associated with haemodynamic improvements combined with positive trends of SOFA score and norepinephrine requirements. Moreover, good renal recovery (82%) and survival rate higher than the SOFA predicted ones (23% vs. 50%) resulted in our population. Although this study has many limitations such as lack of endotoxins levels assessment and no randomization analysis, we believe that it represents a promising result to start further investigations related to the use of this newly developed membrane in post-cardiac surgery patients with AKI and sepsis.

	Before Treatment (mean±STD)	After Treatment (mean±STD)	t-test
SOFA	12.9±2.6	8.2±3.2	p<0.001
MAP (mmHg)	63±17	80±12	p<0.001
Urine Output (ml/12h)	540±570	740±660	p<0.01
Norepinephrine (γ/kg/h)	0.32±0.32	0.04±0.1	p<0.001

#### 54. Use of a Hypertonic CVVHDF Prescription for the Treatment of Diffuse Cerebral Edema in Patients Refractory to Hypertonic Saline Boluses

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##### Purpose:

Current guidelines support the use of hypertonic saline to treat intracranial hypertension. Solutions used range from 3 to 23% saline. Patient's exhibit a rapid increase in serum sodium concentrations and a reduction in cerebral edema which persists over 6 hours. This therapy has demonstrated variability in sodium and chloride concentrations that contribute to the reduction in efficacy 4-6 hours after administration. We hypothesize that a hypertonic saline CRRT prescription can be used to maintain stable serum sodium concentrations in patients who fail to respond to conventional therapy.

##### Experimental Method:

##### Monitoring:

ICP or optic nerve diameter Q6  
CI, SVV, SVI, MAP  
Sodium and pH Q2 via ABG  
BMP Q4  
TCD Q12

##### Targets of therapy:

sodium 155-165 mEq  
serum osmolality 300-340  
chloride <110  
ph 7.3-7.5  
ICP < 20  
CPP > 50

CVVHDF:

Qb Rate: 150 cc/hr

Anticoagulation:

Sodium Citrate 150 mEq/hr

Calcium gluconate at 5 mEq/hr

PBP:

Prismasol 4K/0Ca with 14.6% NaCl (Sodium of 160 mEq/L at 750 cc/hr)

Dialysate:

Plasmalyte with 10cc Sodium Acetate (Sodium of 160 mEq/L at 500 cc/hr)

Replacement Solution:

Prismasol 4K/0Ca with 14.6% NaCl (Sodium of 155 mEq/L at 500 cc/hr)

Summary of results:

CASE 1

An 18 year old male presented with TBI secondary to MVC. Initial optic sheath diameter was 0.80 on right and 0.78 on left. Over 38 hours the patient had a decrease in optic nerve diameter to 0.4 on right and 0.34 on left and an improvement in GCS from 6 to 11. Target serum sodium was attained in 2 hours and was maintained between 155-165.

CASE 2

A 3 year old male presented following MVC. Initial GCS was 8; CT head demonstrated a 4.8 mm right subdural parietal hematoma, with a 3 mm shift. Patient was taken for decompressive craniotomy and a Codmans catheter was placed. Patient was started on intermittent mannitol followed by 7.5% saline, sedated with propofol, and paralyzed. Patient was also initiated on hypothermic protocol. Despite treatment ICP increased to 24, and patient was started on CRRT with a hypertonic prescription. ICP decreased to 10 within two hours of treatment. Patient was continued on the hypertonic prescription for 60 hours. Cerebral blood flow was monitored with TCD which demonstrated an improvement in cerebral perfusion following initiation of therapy.

Conclusions:

Hypertonic CVVHDF can be effectively used in patients with diffuse cerebral edema that fail to respond to bolus hypertonic saline therapy or mannitol.

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## **55. High Cut-Off Hemodialyzers Efficiently Remove Immunoglobulin Free Light Chains And Reduce Tubular Injury Induced By Plasma Of Patients With Multiple Myeloma**

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<sup>1</sup>*Nephrology, Dialysis and Kidney Transplantation Unit, University of Turin, Italy*

**Background and aim of the study:** Patients with multiple myeloma (MM) develop acute kidney injury (AKI) due to free light chains (FLC) deposition in tubular epithelial cells (TEC) with formation of tubular casts and triggering of apoptosis. High cut-off (HCO) hemodialyzers have been shown to remove FLC allowing renal recovery. The aim of this study was to correlate FLC removal by HCO filters with urine NGAL, retinol binding protein (RBP),  $\alpha 1$ -microglobulin ( $\alpha 1$ -M) and with the pro-apoptotic effect of plasma of patients with MM on cultured TEC.

**Methods:** We selected 5 MM patients (IgA $\lambda$  or IgG $\kappa$  type) with AKI (RIFLE criteria) requiring dialysis (HCO Gambro Theralite, 18 sessions of 6 hr, blood flow 300 ml/min, dialysate flow 500 ml/min). Plasma FLC and urine NGAL were analyzed by nephelometry. Urine immunoelectrophoresis was also performed. In vitro on TEC, we evaluated FLC binding by FACS/immunofluorescence, MM plasma-induced apoptosis (TUNEL, caspase-3 activity), mitochondrial function and NGAL mRNA/protein expression.

Results: At study admission, mean serum creatinine was  $6.74 \pm 1.12$  mg/dl, plasma FLC  $10246.53 \pm 2249.38$  mg/L, urine NGAL  $226.73 \pm 41.85$  ng/ml, RBP  $62.82 \pm 12.64$  mg/g creatinine,  $\alpha 1$ -M  $287.28 \pm 39.75$  mg/g creatinine. At day 28 from the inclusion in the study, we found that 4/5 (80%) of MM patients recovered renal function after HCO treatment. After 5 days, we observed the removal of more than 50% FLC and a significant decrease of urine NGAL, RBP and  $\alpha 1$ -M. In vitro, MM plasma induced dose-dependent TEC apoptosis via mitochondrial dysfunction, caspase activation and an increase of NGAL mRNA/protein expression. HCO treatment significantly reduced FLC binding to TEC, MM plasma-induced apoptosis and NGAL up-regulation.

Conclusions: The results of the present study showed that HCO dialysis efficiently remove FLC and reduced MM plasma-induced tubular injury. Urine NGAL, RBP,  $\alpha 1$ -M and in vitro TEC apoptosis are useful biomarkers to evaluate FLC removal by HCO filters, tubular injury and renal recovery.

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## 56. Effective Dose, Defined as Urea Reduction Ratio during First 24 Hours of CRRT, Could Reduce Mortality in Patients with Septic Acute Kidney Injury

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Background: Prescription dose or delivery dose of continuous renal replacement therapy (CRRT) was not related to the mortality in patients with acute kidney injury (AKI) in recent studies. However, some previous studies showed that a greater intensity of CRRT significantly reduced the mortality of them. Considering the critical catabolism of individual patients with septic AKI, a greater effective dose accompanying high urea reduction ratio during first 24 hours of CRRT may be associated with an improvement of mortality.

Objectives: We investigated whether a greater effective dose was related to the lower in-hospital mortality because lower in-hospital mortality could lead to an improvement of 28-day or 90-day mortality rates.

Methods: We analyzed prospectively collected data to elucidate the relationship between the effective dose and in-hospital mortality in 53 patients (M:F=38:15, age  $62.2 \pm 11.0$  years) with septic AKI requiring CRRT. Continuous venovenous hemodiafiltration (hemodialysis: hemofiltration=50: 50) was prescribed to all subjects to provide a total effluent of 40 ml/Kg/hour. Effective dose was defined as urea reduction ratio during first 24 hours of CRRT. RIFLE criteria at the initiation of CRRT and the effective dose were evaluated.

Results: Overall mortality rate was 41.5% (22/53). There was no significant difference of baseline characteristics at the initiation of CRRT between survival group and non-survival group in age (63(28-79) years vs. 67(40-76) years,  $p=NS$ ), sex (M:F=21:10 vs. M:F=17:5,  $p=NS$ ), BUN (43(7-122) mg/dL vs. 30(12-135) mg/dL,  $p=NS$ ), APACHE II (27(12-43) vs. 29.5(19-45),  $p=NS$ ) and SOFA scores (12(6-20) vs. 14(8-19),  $p=NS$ ). However, RIFLE classification revealed more severe renal dysfunction in survival group (injury: failure=14/31(45%): 17/31(55%)) than in non-survival group (injury: failure=16/22(73%): 6/22(27%),  $p=0.048$ ). Nonetheless, the effective dose was significantly greater in survival group (46.5 (-33~74) %) than that (27.3 (-92 ~ 65) %) in non-survival group ( $p=0.040$ ).

Conclusions: The effective dose to overcome a critically hypercatabolic individual status of a patient with septic AKI could be an index to improve mortality. In the future, it is necessary to confirm whether the effective dose > 50% would reduce mortality in a large prospective randomized controlled trial.

## 57. Single Pass Albumin Dialysis (SPAD) in Pediatric Patients with Hyperbilirubinemia on CRRT.

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Hyperbilirubinemia occurs in critically ill pediatric patients needing Continuous Renal Replacement Therapy (CRRT) in the ICU. The Molecular Adsorbent Recirculating System (MARS) dialysis has been described in patients with fulminant liver failure. However MARS is available in limited pediatric centers. There is little published data on using albumin in commercially available dialysate solutions for Single Pass Albumin Dialysis (SPAD). We describe the use of albumin as a dialysate additive in two pediatric patients with hyperbilirubinemia.

At our center, dialysate is delivered via a weight based CRRT machine (Gambro-Prismaflex). The dialysate bag weight is limited to 5L. Albumin was ordered as grams/dL, with pharmacy displacing the volume of dialysate with an equal volume of albumin. The bedside nurse weighed each bag of dialysate/Albumin and removed any excess over 5 liters before placing the solution on the pump. Both received CVVHDF with the dialysate/Albumin solution for 36-48 hours followed by CVVHDF with standard solutions.

Patient A was a 12 year old male bone marrow transplant patient with sepsis admitted to the Pediatric Intensive Care Unit (PICU) on Hospital Day 9 and CRRT started on Day 37. Total parenteral nutrition (TPN) was used >30 days prior to CRRT. Total Bilirubin (0.1-1.3mg/dL) was 1.04 on admission to the hospital, rose to 8.97 on PICU admission, 3.4 on CRRT initiation, and was 20.22 when albumin was added to the dialysate. When the bilirubin fell to 16.31, albumin was removed.

Patient B was a 3 day old male admitted to the PICU with Persistent Pulmonary Hypertension of the Newborn (PPHN) and initiated on Extracorporeal Circuit Membrane Oxygenation (ECMO) on hospital day 6. CRRT with albumin was started on hospital day 15. Total Bilirubin was 10.60 on admission, and rose to 44.10 on initiation of CRRT with albumin 19.10 when albumin was removed.

This method of CRRT worked well but does pose potential problems. Albumin is costly and in limited supply and like MARS likely works best in short duration times like 6-8 hours. Centers using a weight based system for CRRT may have problems with the added weight of albumin. Pharmacy resources may also be limited. While both patients ultimately expired, there may be potential benefit to initiate this method earlier in the ICU stay.

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## 58. Can We Achieve Optimal Ultrafiltration In End Stage Heart Failure Patients With LVAD Who Develop AKI And Fluid Overload Requiring CRRT?

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Left ventricular assist device (LVAD) implantation is used to bridge patients with end-stage heart failure (ESHF) to cardiac transplantation or as destination therapy. Continuous renal replacement therapy (CRRT) is challenging in LVAD patients with acute kidney injury associated with fluid overload. A close collaboration between nephrologists and cardiac surgeons is essential to optimize fluid status. A protocol based ultrafiltration (UF) was developed in this setting. Daily Continuous CVP and MAP monitoring parameters were used during CRRT. Since the right heart is at risk of failing due to fluid overload in LVAD patients, CVP was selected as the main criteria for UF. UF was done while maintaining MAP > 60 mm Hg by vasopressors or titrating LVAD parameters If CVP was > 15 cm H<sub>2</sub>O. If CVP was < 12 cm H<sub>2</sub>O, no UF was done unless MAP is >60 mm Hg and a clinical evidence of fluid overload. We collected data retrospectively on 17 ESHF patients (Mean age 60±9 (SD), range 45-76 years, 13 M and 4 F) who underwent HeartMate II LVAD implantation from April 2010- June 2012. 11 patients had CKD (eGFR < 60 ml/min/1.73 m<sup>2</sup>) prior to LVAD placement. 8 patients developed AKI, of these 3

patients (mean age 70, range 68-72 years, 3M) required CRRT over a total number of 68 days. A complete data set was available on 55 days. CRRT was done using the Prisma M100 set with AN69 hemofilter with citrate anticoagulation. Data are summarized in the table:

The mean delivered UF rate (52.9+81.7 ml/hr) was significantly ( $p<.01$ ) lower than the mean prescribed UF (70.4+54.0 ml/hr). The prescribed UF correlated significantly ( $p<.05$ ) with MAP. However no significant relation was observed between delivered UF and MAP. Similarly, no correlation was found between CVP and prescribed or delivered UF. UF rate of >50 ml/hr in patients with CVP >15 cm H<sub>2</sub>O was not prescribed in 3 of 10 days on CRRT while was not delivered on 2 of 10 days. Data suggest that protocol with a single target parameter as priority e.g. continuous CVP or MAP monitoring if available for UF, can improve in optimizing volume status in patients with LVAD requiring CRRT.

No of days: 55	Prescribed UF ml/hr	Delivered UF ml/hr	CVP cm H <sub>2</sub> O	MAP mm Hg	BUN mg/dl	Serum creatinine mg/dl
Mean + SD	70.4+54.0	52.9+81.7	13.8+2.4	61.9+6.1	45.0+17.3	1.44+0.68

## 59. Non-renal Indication of Renal Replacement Therapy in a Patient with Sickle-cell Associated Fulminant Liver Failure and Thrombocytopenia Associated Multi-organ Failure (TAMOF)

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3 yr old female with sickle cell disease maintained on chronic transfusion and iron chelation presented to emergency center with abdominal pain, vomiting, fatigue and wobbly gait with increased sleepiness. On exam, she was obtunded with GCS of 8, had lower extremity hypertonia and hyperreflexia with positive Babinski's. Stroke protocol imaging and sepsis work up was negative. She was admitted to the ICU after intubation for altered mental status. Further work up revealed acute non oliguric kidney injury (AKI) with serum creatinine of 1.66 mg/dL and hyperammonemia to 290 mcumol/L. She was started on CVVHDF for hyperammonemia with improvement in ammonia levels and CVVHDF was discontinued after 16 hours. However, elevated transaminases with worsening coagulopathy and further deterioration in the neurological status was compatible with a picture of hepatic encephalopathy. Serum creatinine peaked at 2.5 but she remained nonoliguric. On hospital day 3, she had splenic sequestration with acute hemodynamic decompensation requiring escalating vasoactive support and developed acute respiratory distress syndrome (ARDS) necessitating HFOV. Clinical picture was thought consistent with Thrombocytopenia-associated Multiple Organ Failure (TAMOF) with platelet counts < 100K/mm<sup>3</sup> and six failing organs (Liver, cardiac, respiratory, renal, hematologic, and neurologic failure). Patient received therapeutic plasma exchange with centrifugation apheresis for 5 days. After first treatment, coagulopathy improved and she was taken off all pressors after 3 treatments. Liver enzymes and creatinine started to normalize and she was weaned off HFOV by the end of the pheresis course. No further renal replacement therapy was required. She was eventually extubated and discharged home. Further inquiry revealed patient had received double the dose of desferisirox for iron overload in the week prior to presentation, which has been reported to cause AKI and drug induced hepatitis and was speculated to be the likely etiology in this patient with sickle cell disease. We report successful utilization of CVVHDF and daily plasma exchange to correct hyperammonemia in desferoxamine induced toxic fulminant acute liver failure in a pediatric patient with comorbid sickle cell disease. This is the first report of desferoxamine in children leading to acute liver failure and AKI leading to TAMOF.

## 60. MANAGMENT OF AKI IN NEWBORN WITH MINIATURIZED EQUIPMENT FOR CRRT (CARPEDIEM). FIRST WORLD CASE REPORT

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**BACKGROUND** Continuous renal replacement therapy (CRRT) is becoming the treatment of choice to support critical pediatric patients with AKI, fluid overload (FO) and hemodynamic instability. This therapy is usually performed with machines designed for adults. In these patients mortality is associated with the presence of MODS, patient weight, and the severity of FO. We report the first patient treated with the Carpediem, CardioRenal Pediatric Dialysis Emergency Machine, a newly miniaturized equipment designed for neonates: this is a case of an infant with severe FO who received CRRT primarily to remove fluid excess. **CASE REPORT**

Patient 38 week-old male infant (3.2 kg) was transferred from a community hospital and admitted to the PICU with sepsis and acute lung injury due to severe combined immunodeficiency syndrome. Medications include 2 inotropes and almost one potential nephrotoxic agent (aminoglycosid). He was sedated and intubated 10 hours after admission. Adequate diuresis was always maintained with continuous infusion of diuretics. The degree of FO was 24% of body weight on the Day 4 (Fig1), pRIFLE R, increasing to 30% before CRRT initiation, pRIFLE R. Concomitant with bone marrow transplantation on Day 6, fluid intake fell to 709 ml/day, and patient had a further decline in renal function, reaching pRIFLE I on Day 9. Urine output decreased and to reduce the degree of FO, a total of 500 ml/day was removed with CRRT. To avoid common complications such as: temperature, vascular access, excess of extracorporeal priming volume, the CaRPeDiEM was utilized. Pre-dilution CVVH was performed for 61 hours without significant hemodynamic disturbance, technical complications or need for more inotropic agents. Heparin was continuously infused. Blood pressure was stable, particularly around the time of CRRT initiation (fig2), without any hypotension episode for all the entire duration of CRRT. No clotting occurred in the extracorporeal circuit thanks to accurate anticoagulant monitoring. The main reason for CRRT discontinuation was recovery of renal function. Patient died 2 days after for respiratory failure. FO was reduced by 17% over the 61 hours of CRRT. **CONCLUSIONS** A critically ill newborn underwent CRRT with CARPEDIEM, showing an improvement of cardiac, pulmonary and hemodynamic parameters, maintaining optimal fluid and circulatory stability. CARPEDIEM can be an effective CRRT machine for small size infants, avoiding typical complications and risks due to the adults machine use

Figure 1. Trend of UO, Drugs and FO(%) with pRIFLE classification

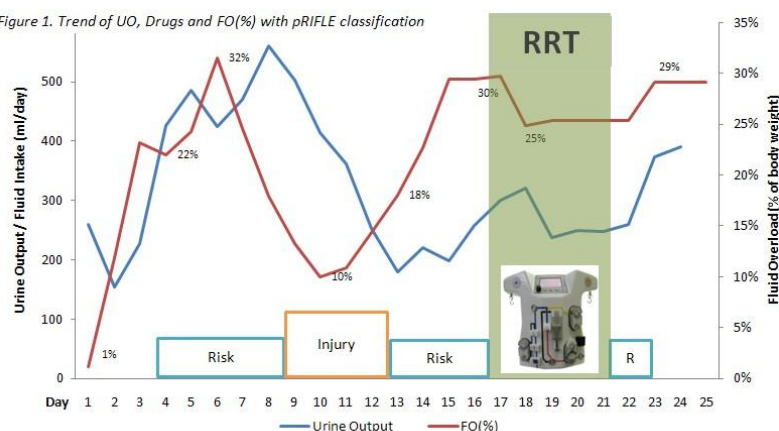
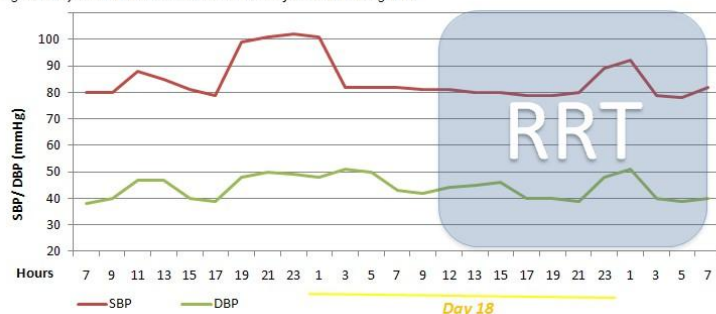


Figure 2. Systolic and Diastolic Pressures before and during RRT





## 61. Urological Surgical Sequels Impact the Renal Functions-3 Critical Cases Analysis

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Endoscopic bladder or prostate surgeries will cause uncommon acute renal failure situations that might relate to intraoperative sepsis or TUR syndrome, we reported 3 critical cases and the share managing strategies.

Case 1: A 77 years old male patient had suffered from septicemia and septic shock post TUR-P due to acute infectious sources reflux into the venous plexus during the operation. The critical condition caused acute renal failure, hemodialysis rescued the renal function successfully.

Case 2: A 85 years old female patient had suffered from bladder perforation when transurethral resection of bladder tumor, and it led to hypo-osmolality hemodynamic change due to distilled water intraperitoneal influx and absorption. Followed by hemolysis and acute renal failure, hemodialysis was applied to rescue the renal function successfully.

Case 3: A 78 years old male patient had suffered from bladder perforation during performing the transurethral resection of bladder cuff before nephroureterectomy, it caused hypo-osmolality hemodynamic change due to distilled water intraperitoneal influx and absorption. Followed by hemolysis and acute renal failure, hemodialysis was applied to rescue the renal function successfully.

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## 62. Slow Low-Efficiency Renal Dialysis to Initiate Renal Replacement Therapy for Chronic Uremia

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### Introduction:

Slow low-efficiency dialysis (SLED) is an accepted modality of renal replacement therapy (RRT) in the intensive care unit setting. For chronic uremia, it is customary to start new inpatients on RRT with an escalating daily regimen (2 hours 1st day; 3 hours 2nd day; 4 hours on the 3rd) to avoid dialysis disequilibrium syndrome. However, this approach may prolong inpatient admissions and delays chronic outpatient dialysis placement.

### Methods:

We reviewed our experience with 7-8 hours SLED in the in-center hospital setting to initiate RRT for patient with newly declared clinical uremia. During these initial treatments, temporary accesses were utilized with flow set at 200 mL/min, counter-current flow at 100 mL/min (Na<sup>+</sup>140 mM/L, HCO<sub>3</sub><sup>-</sup> 30 mM/L). We reviewed multiple biochemistry studies both before and after SLED treatment (immediate and up till 4-12 hours, as available), including for osmolality (Osm), Blood Urea Nitrogen (BUN), serum creatinine (Cr), sodium (Na<sup>+</sup>), bicarbonate (HCO<sub>3</sub><sup>-</sup>) and phosphorus. Urea Reduction Ratio (URR) was calculated from BUN values obtained before and after RRT in a standardized manner. Results are listed with means (±SD).

### Results:

We identified four patients, who presented with renal failure of uncertain duration and received SLED modality to initiate RRT; three of them were discharged with final diagnosis of End-Stage Renal Disease. Of the patients, 3 received treatments for 8, one for 7 hours. Baseline studies included BUN 124.5 (21.4) mg/dL, Cr 10.72 (5.26) mg/dL, HCO<sub>3</sub><sup>-</sup> 16 (2.8) mM/L, Na<sup>+</sup> 127.5 (8.2) mM/L and Osm 330 (23.4) mOsm/kg. URR of this single SLED was 70.7 (3.3) % (range: 67-74). Follow-up studies revealed BUN 43.5 (9.1) mg/dL, Cr 4.44 (2.26) mg/dL, HCO<sub>3</sub><sup>-</sup> 23.3 (2) mM/L, Na<sup>+</sup> 130.2 (3.5) mM/L, Osm [3 subjects only] of 283.3 (10) mOsm/kg, four hours after treatment. Phosphorus clearance was also excellent with baseline of 6.8 (1.9) mg/dL dropping to 4.1 (1.9) [varying times, four to 12 hours after treatment]. No patient experienced any side effect despite excellent clearances with SLED modality.

#### Conclusion:

In our case series, upfront SLED was very effective and well tolerated in chronic uremia. Despite the marked drop of BUN and osmolality, no dialysis disequilibrium was observed clinically. This approach needs to be studied in larger cohorts or formal trials.

Lab	Pre-SLED	Post-SLED
Blood Urea Nitrogen	124.5 (21.4) mg/dL	43.5 (9.1) mg/dL
Creatinine	10.72 (5.26) mg/dL	4.44 (2.26) mg/dL
Osmolality	330 (23.4) mOsm/kg	283.3 (10) mOsm/kg
Bicarbonate	16 (2.8) mM/L	23.3 (2.0) mM/L
Sodium	127.5 (8.2) mM/L	130.2 (3.5) mM/L
Phosphorus	6.8 (1.9) mg/dL	4.1 (1.9) mg/dL

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### 63. Sodium Modeling During Controlled Hypertonic CVVHD for ICP Management Using a Multiscale Mathematical Model

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**Purpose:** Manipulation of serum and extracellular electrolytes is an important part of the management of critically ill patients. Controlled hyponatremia can play a role in the management of intracranial hypertension. The ability to predict CRRT operating parameters and/or results of therapy may prove useful in the application of this therapy.

**Methods:** A multiscale mathematical model was developed for the simulation of citrate and bicarbonate dynamics, and previously presented (CRRT 2012). This model consisted of a finite element analysis (FEA) model based on partial differential equations for fluid and solute handling in hemofilter hollow fibers, coupled to a multiple compartment model based on ordinary differential equations that describes the dynamics of fluid and solute handling in the body. The FEA model incorporated hemofilter blood and dialysate flow, protein transport and osmotic pressure, solute reflection, and diffusive and convective solute transport under variable operating flow and pressure conditions. The compartment model incorporated distribution, transport and elimination processes in body compartments for citrate, bicarbonate, and selected solutes. For this project, the model was extended to include sodium modeling for prediction of serum sodium levels during hypertonic CVVHD applied in two patients for the induction of controlled hyponatremia in management of intracranial hypertension. The existing model was expanded to include sodium transport in citrate anticoagulant, pre- and post-dilution replacement fluid, and dialysate. Intra- and extracellular sodium compartments were added to the compartment model.

**Results:** Two patients (70 kg and 23 kg) with intracranial hypertension were managed with elevated serum sodium levels using CVVHD with 4% sodium citrate, and the sodium concentration in replacement fluids and dialysate were increased to 160 mM/L. Sodium was monitored every 2-4 hours. Simulations over the initial 8 hours were run on each of the two patients using the same operating conditions. Comparison of recorded and predicted sodium levels revealed good agreement over the simulation period.

**Summary:** This multiscale model can provide reasonable prediction of sodium levels over brief periods of time during hypertonic CVVHD. Prolonged agreement may not be possible due to sodium and water dynamics not included in the model, such as insensible and urine losses, and non-CRRT intravenous fluids.

#### 64. Complications of Continuous Renal Replacement Therapy: A retrospective cohort study

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<sup>1</sup>Mayo Clinic

**Purpose:** AKI is a common and life-threatening complication in critically ill patients.. The use of continuous renal replacement therapy (CRRT) is frequently employed for AKI patients with severe renal dysfunction. The evidence on the incidence of CRRT complications is mostly in the form of case reports and there has not been a comprehensive systematic review o evaluation of the complications in a large cohort. Therefore, we aimed to determine the incidence of mechanical, metabolic, and hemodynamic complications of CRRT.

**Methods:** We conducted a retrospective cohort study, evaluating all of the consecutively admitted adult patients (≥ 18 years) who underwent CRRT from December 9, 2006 to December 31, 2009 in the ICUs at the Mayo Clinic, Rochester, MN. We evaluated the incidence of the complications that are directly or indirectly related to CRRT.

**Results:** Of 595 patients who underwent CRRT, 229 (38%) were women, 485 (82%) were white. The median age was 62 years (IQR, 52-72). The median Charlson index score, SOFA score and APACHE III score on the day of ICU admission were 3 (IQR, 1- 5), 10 (IQR, 6 - 14) and 114 (IQR, 96-133), respectively. The median ICU and hospital length of stay for patients undergoing CRRT were 8.9 days (IQR, 4.2-16.8) and 21.5 days (IQR, 9.9 – 39.0) days, respectively. The median duration of CRRT was 4.0 (IQR, 1.8-7.3) days. The main reason for CRRT initiation was AKI (n = 553, 93%) and the most common predisposing factors for AKI were sepsis (n=257, 46%), cardiorenal syndrome (n=101, 18%), post-surgical (n=96, 17%), and contrast-induced (n=16, 3%). A total of 43% of patients developed hypotension within 1 hour of CRRT initiation. The most common electrolyte complications during CRRT were hypocalcemia (92%), hyperphosphatemia (67%), hypercalcemia (62%), hypophosphatemia (58%), hypokalemia (45%), hypermagnesemia (39%), hypomagnesaemia (32%), hypernatremia (29%), hyperkalemia (26%), and hyponatremia (25%) respectively. A total of 23% patients had bleeding as a complication during the insertion of catheters and the maintenance of CRRT, ICU and hospital mortality rate of 40% and 51%, respectively.

**Conclusions:** AKI is the most important cause for CRRT initiation. AKI patients who required CRRT had a high mortality. Hemodynamic and electrolytes imbalances are very common during CRRT. Future studies should focus on identification and prevention of these factors.

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## NEW TECHNOLOGY

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#### 65. Simplified Regional Citrate Anticoagulation Using a Calcium-containing Replacement Solution for Continuous Venovenous Hemofiltration

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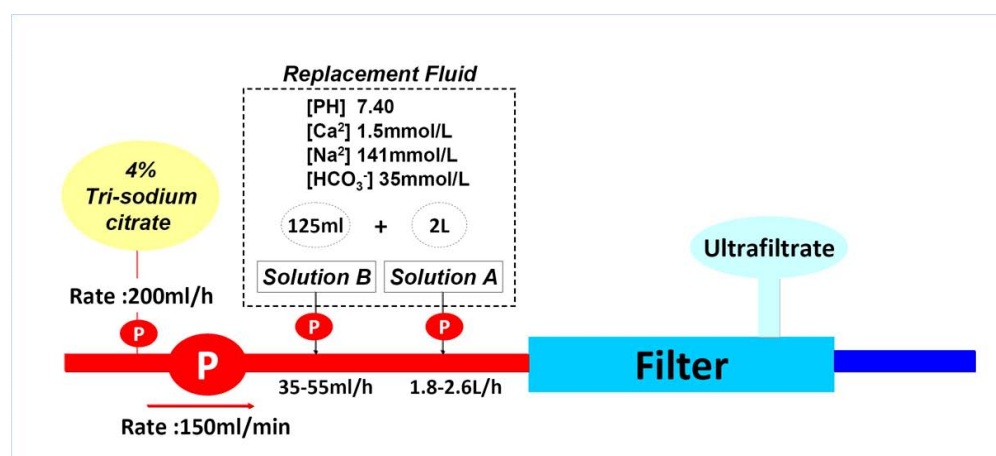
<sup>1</sup>West China Hospital of Sichuan University, Chengdu, Sichuan, China

**Objective :** Regional citrate anticoagulation (RCA) is an effective and safe method for continuous renal replacement therapy (CRRT) , but RCA is not widely used because of complex therapeutic modalities and specialized calcium-free replacement solution with the need of continuous intravenous calcium infusion. We designed a simplified protocol for RCA by using an available calcium-containing replacement solution for continuous venovenous hemofiltration (CVVH).

**Methods :** Twenty-six patients, with acute or chronic renal failure in the intensive care unit of West China Hospital of Sichuan University, were treated with RCA-based pre-dilution CVVH using a calcium-containing replacement solution (ionized calcium 1.50mmol/L). We pumped the 4% tri-sodium citrate solution into the arterial line of extracorporeal circulation with a starting rate of 200ml/h , while adjusting the rate to achieve a post-filter ionized calcium level between 0.25 and 0.5mmol/L. Initial blood flow was set at 150ml/min. The replacement solution was delivered at 35ml/kg/h. Biochemical parameters , arterial blood gas analysis and whole blood activated clotting time (WBACT) were assessed. We also measured the serum and effluent citrate concentration during CVVH at 0, 24, 48 and 72h.

**Results :** We performed 148 sessions. Mean hemofilter survival was  $61.3 \pm 21.6$ h (range, 14-122h). Mean 4% tri-sodium citrate solution pumped was 207 (190-230) ml/h, and mean pre-filter and post-filter ionized calcium level were 0.96-1.02 mmol/L and 0.34-0.38 mmol/L respectively. Ninety-two percent, 63%, and 48% of hemofilters were patent at 24, 48, and 72h. The pre-filter WBACTs altered little ( $P > 0.05$ ) , but the WBACTs of post-filter significantly prolonged about 30% compared with that of pre-CVVH ( $P < 0.05$ ). The mean serum citrate concentration was not changed significantly at 24, 48, and 72h. No bleeding episodes were found, and no patient showed the symptoms and signs of hypocalcium or citrate toxicity.

**Conclusions :** Our simplified RCA protocol using a calcium-containing replacement solution for CVVH is effective and safe and also obviates the need of continuous intravenous calcium infusion.



## 66. Successful Treatment of Hepatorenal Syndrome With Continuous Flow Peritoneal Dialysis (CFPD) Using a Dual Lumen Ronco Catheter

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**Purpose:** Hepatorenal syndrome (HRS) is a well known cause of acute kidney injury (AKI) associated with high morbidity and mortality. Renal replacement therapy (RRT) for HRS is often not considered in patients who are not candidates for liver transplantation. Conventional modes of RRT may be hemodynamically intolerable in patients with HRS. We report the successful treatment of a patient with cirrhosis and HRS with CFPD.

**Methods:** A 62 year old alcoholic cirrhotic man with tophaceous gout, presented to our MICU with hypotension, tense

ascites, anasarca, cachexia, bright red blood per rectum, oliguria, and rising serum creatinine. He was treated with blood transfusion, IV albumin, midodrine, octreotide, and norepinephrine. Serum creatinine continued to rise, tense ascites reaccumulated post paracentesis, and he was dyspneic at rest. His condition deteriorated with obtundation, worsening anasarca and acidemia. He was not a transplant candidate, hemodynamically unstable, and palliative care was discussed. CFPD was suggested and family agreed. A Ronco dual lumen catheter was available and we placed this at bedside. Initially, standard acute PD was performed, as we could not verify intraperitoneal positioning of diffuser portion of catheter. He improved, but was hypotensive due to negative balance 4-7 L/day. Catheter position verified radiographically and CFPD initiated after 2 weeks standard PD. We used Fresenius 2008H to dialyze ascites at Qp of 300 ml/min. External dialysate flow (Qd) set at 500 ml/min. Ascites removed by ultrafiltration of 2-4 liters/session. Each session lasted 4-6 hours, and we ran from 4-6 sessions per week. Pre and post-Rx blood chemistries were drawn and used to calculate clearances using the Daugirdas equation.

Results Summary: Patient improved clinically over several weeks with clearing of anasarca (20 kg net weight reduction), control of ascites, acidosis, and withdrawal of pressors. Kt/V urea averaged 0.25 per Rx (see Table) with mean urea clearance (Ku) of 46 ml/min. He remained cachectic, and sessions increased to 6 hours. Ku declined after 6 months to 20 ml/min. HD added to improve clearance, but he developed refractory GI bleeding and expired 8 months after beginning RRT.

Conclusion: CFPD via the Ronco catheter was extremely successful as RRT in a severely ill cirrhotic, ascitic patient with HRS.

Date	Wt pre (kg)	Wt post	Vol (L)	Rx time (min)	Qp	UF vol(ml)	Pre BUN	Post BUN	KuT/V	Ku
25-Apr	81.4	77	48.8	240	300	3961	27	23	0.25	50.9
26-Apr	79.4	77.6	47.6	240	300	1800	24	21	0.21	41.7
28-Apr	78	77.3	46.8	245	300	1000	27	23	0.21	40.1
30-Apr	78.8	77.3	47.3	240	300	1500	30	24	0.32	63.0
7-May	75	71.8	45	260	200	3200	48	41	0.24	41.5
17May	69.9	66.7	41.9	260	300	3065	34	29	0.25	40.3
Mean						2421			0.25	46.3

## 67. FIRST WORLD APPLICATION OF CARPEDIEM (MINIATURIZED CRRT EQUIPMENT FOR INFANTS): A TECHNICAL EVALUATION

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<sup>1</sup>St. Bortolo Hospital, Vicenza, Italy

Acute kidney injury (AKI) is an independent risk factor for morbidity and mortality in critical ill children. Renal replacement therapy (RRT) is a cornerstone of therapy to correct uremia and fluid overload. Provision of maintenance hemodialysis to neonatal and infants implicate many challenges: blood flow rate, UF settings and accuracy, catheter size and length, extracorporeal circuit volume, circuit functional survival and the anticoagulation strategy.

Aim

We evaluated the technical aspects of the first world in-vivo treatment with the new cardio renal paediatric dialysis machine (CaRPeDiEM) specifically designed for infants.

Material and Methods

Patients weighting 3.2 Kg admitted at the PICU, was treated with the CaRPeDiEM in CVVH pre dilution. Fluid overload was the main reason for RRT initiation. The extracorporeal circuit included a D50 hemofilter (polysulfone, 0.075m ) totalizing 27ml of priming volume (10% of total circulating blood volume) A 4.5 FR dual lumen catheter length 3.9 inch was

placed in the femoral veins. Heparin was continuously infused of 10 U/kg/hr. Haemoglobin was 10 g/dL.

#### Results

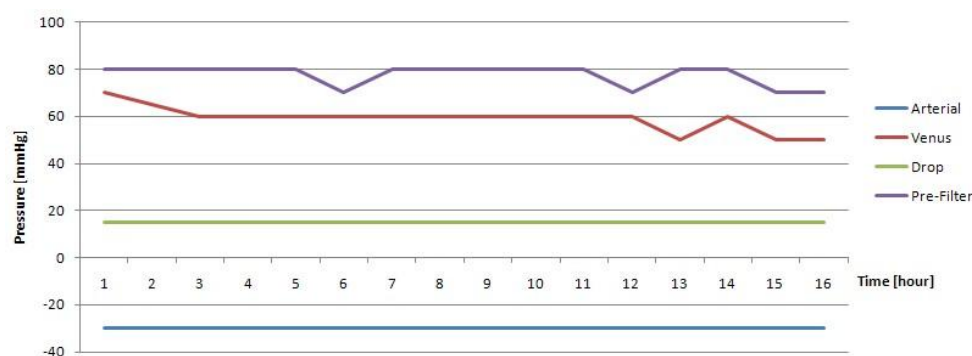
A total number of 61 hours was done with 4 circuits. Arterial, Venus, Drop and PreFilter Pressures were stable during all treatment (see figure 1 for the first circuit, 16h).

#### Discussion

Despite the negative data in literature ( $13.9 \pm 8.6$  h with 6.5 FR catheter for patients weighting  $< 3$  Kg or circuit life  $< 20$  h with 5 FR catheter, PPCRRT Registry) our circuit life was quite long ( $17.5 \pm 6.24$  h). In addition the reasons for downtime were clinical. Limitation on flow through a tube described by Poiseuille law and the need of laminar flow dictated by Reynolds, suggest the right blood flow need to optimize the circuit survival, in particular with small catheter. The Carpediem blood pump allows a wide and appropriate range (5-50ml/min) of flows. Fluid balance safety is moreover assured by a very high sensitivity, 1g, scale.

#### Conclusion

The data of the first in vivo treatment, suggest that CRRT with Carpediem is safe and effective in neonates and infants weighting less than 10 Kg. Prolonged circuit survival with small catheter due to equipped features, allows to explore all potential benefits of CRRT in infants without technical and clinical complications.



## 68. Mesenchymal Stem Cell Devices for the Treatment of AKI

Biju Parekkadan<sup>1</sup>

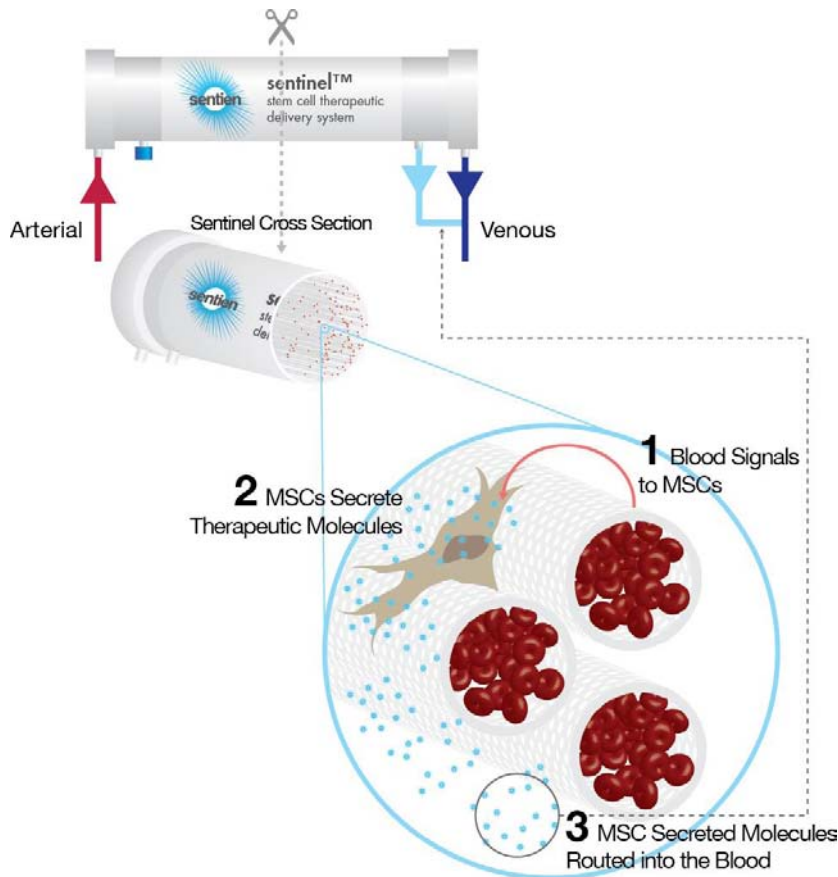
<sup>1</sup>Sentien Biotechnologies, Inc., Medford, MA, USA

Cell therapy offers a unique opportunity to deliver broad support for patients with AKI. Bone marrow-derived mesenchymal stem cells (MSCs) are an excellent candidate for human cell therapy. MSCs are naturally tissue-protective and are under intense evaluation for the treatment of many conditions, including kidney disease. A major gap that has prevented the use of MSCs for renal care is the suboptimal delivery of this therapy.

We have evidence that MSC therapy is due to a combination of metabolic and secreted factors stimulated by blood that protect tissue cells and reduce inflammation. Sentien Biotechnologies, Inc. was formed to create an engineered, blood-contacting bioreactor to optimize MSC metabolism and secretion for clinical use. MSCs are inoculated into a high-flux dialyzer as a platform to continuously allow MSCs to interact with blood in high fidelity. In these devices, adherent MSCs are separated from blood by a permeable membrane and do not enter the subject, thereby eliminating concerns of exposure to foreign cells. These cellular devices (termed Sentinel™) increased survival by a 5x over MSC transplants in a model of inflammatory organ failure. We have scaled up the technology to a human prototype that has sustained cell viability and function throughout manufacturing and in vivo operation. A panel of MSC metabolic enzymes and secreted factors that have pleiotropic action on immune and tissue cells are used for potency quality control. Our high-flux bioreactor is well tolerated and initial efficacy testing in dogs with kidney ischemia/reperfusion injury has been promising in terms of survival and end



organ protection. Importantly, our devices integrate seamlessly within the current dialysis infrastructure in the clinic with few modifications to existing protocols, which will reduce the barriers to adoption and provide patients with both filtration and immunomodulatory therapy in a single session. We are poised to translate our approach in pursuit of a human trial in the next year.



## RRT RESEARCH

### 69. Outcomes of AKI patients with and without cancer requiring CRRT : A Single Center Study

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<sup>1</sup>Kosin University College of Medicine, Department of Internal Medicine, Division of Nephrology

Background: Up to half of cancer patients experience acute kidney injury (AKI) and the majority of them require renal replacement therapy while in ICU.

AKI in these patients occurs either as a consequence of the cancer itself, anticancer treatments or diverse-associated severe clinical conditions.

Although survival seems to be improving over the last decade, the development of AKI in critically ill cancer patients remains associated with high mortality rates. Few studies have examined the characteristics and outcomes of AKI patients with and without cancer requiring CRRT. The purposes of this study were to evaluate and compare the characteristics and outcomes of cancer and non-cancer patients with AKI requiring CRRT, to determine the impact of cancer diagnosis on hospital mortality; and to compare outcome predictors between the two groups of patients

**Methods:** We evaluated patients with AKI who were treated in ICU of Kosin University Gospel Hospital from January 1, 2010 to December 31, 2011. A total of 200 consecutive patients (without cancer 79%; with cancer 21%) were included over a 48 month period. Predictors of all-cause death were examined using the Kaplan-Meier and Cox proportional hazards analyses in both treatment groups

**Results:** The main contributing factors of AKI were sepsis (38%) and cardiac dysfunction (40%). AKI was multifactorial in 78% of cancer patients and in 71% of patients without cancer. Hospital mortality rates were higher in patients with cancer (69%) than in patients without cancer (49.4 %) ( $P = 0.023$ ). In multivariate analyses, the results showed that gender, presence of cancer and number of failed organs were significant predictors of mortality. The diagnosis of cancer was independently associated with mortality [odds ratio = 1.971 (95% confidence interval, 1.051–3.697),  $P = 0.035$ ].

**Conclusions:** Hospital mortality rates were higher in patients with cancer than in patients without cancer. Gender, presence of cancer and number of failed organs were significant predictors of mortality.

**Table 1. Characteristics of Patients Treated with CRRT**

No. of patients	Non-Cancer (n=158)	Cancer (n=42)	P value
Male:Female	84:74	31:11	0.016
Age, year (range)	65.8 ± 13.0	65.2 ± 10.3	0.771
CKD (%)	58 (36.7)	11 (26.2)	0.202
Death (%)	78 (49.4)	29 (69.0)	0.023
Cause of death (%)			
MOF	37 (51.4)	20 (74.1)	0.002
Cardiac	25 (34.7)	2 (7.4)	
Cerebral	5 (6.9)	0 (0)	
Respiratory	5 (6.9)	2 (7.4)	
Tumor recurrence	NA	3 (11.1)	
Clinical setting			0.861
Medical (%)	123 (78.2)	32 (76.9)	
Surgical (%)	35 (21.8)	10 (23.1)	
Form of admission			0.026
Unscheduled operation	23 (15.0)	1 (2.6)	
Medical	123 (78.2)	32 (76.9)	
Scheduled operation	32 (6.8)	9 (20.5)	
Oliguria (%)	96 (60.8)	26 (63.2)	0.794
Mechanical ventilation (%)	111 (70.1)	24 (57.9)	0.151
Vasoactive drug (%)	101 (64.1)	27 (64.1)	1.000
Bleeding tendency (%)	71 (44.9)	19 (45.9)	0.912
Sepsis (%)	82 (52.1)	31 (74.4)	0.013
Underlying disease (%)			0.043
No	44 (27.8)	21 (50.0)	
DM	72 (45.6)	13 (31.0)	
HBP	30 (19.0)	8 (19.0)	
LC	11 (7.0)	0 (0)	
Heart disease	1 (0.6)	0 (0)	
No. of organ failure (range)	1.3 ± 0.8	1.5 ± 0.5	0.338
Renal function at initial dialysis			
Urine output, mL/24 hrs	656 ± 845	579 ± 626	0.604
BUN, mg/dL	53.8 ± 30.1	71.5 ± 39.5	0.002
Serum creatinine, mg/dL	4.2 ± 3.0	4.3 ± 2.4	0.805

## **70. AN69 membrane improved vascular endothelial functions by decreasing the serum level of MCP-1 on hemodialysis patients.**

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<sup>1</sup>Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, <sup>2</sup>Hemodialysis center, Ako central hospital

**PURPOSE:** It is well known that hemodialysis patients have high risks for cardiovascular disease. The AN69 membrane is known as a new membrane resulting from coating polyethyleneimine upon the polyacrylonitrile surface, binds heparin. There are some reports that AN69 membrane affected some cytokines that relate to vascular functions. However, there is no report that whether AN69 membrane effected to vascular endothelial cell function or not.

**METHODS:** Eleven hemodialysis patients were enrolled in this study with IC. The hemodialysis patients undertook hemodialysis with polysulfone membrane (PS) or cellulose triacetate membrane (CTA). After evaluation the endothelial functions, the PS or CTA membranes were changed to AN69 membrane on hemodialysis. We evaluated MCP-1, NO<sub>3</sub>- and other inflammatory cytokines from serological analysis, and endothelial function by calculating flow mediated dilation (FMD%) and pulse wave velocity (PWV) at before and after hemodialysis.

**RESULTS:** The clinical symptom, such as peripheral coldness or numbness of inferior limb decreased on AN69 membrane compared to PS or CTA membrane. There was no significant decreased change of the serum level of NO<sub>3</sub>- between before and after of hemodialysis (the decreasing rate of NO<sub>3</sub>- in PS or CTA membrane group vs. AN69 membrane group; -66.45 +/- 23.31 % vs. -70.72 +/- 9.88%). However, the serum level of MCP-1 on AN69 membrane group were significantly decreased lower than those of PS or CTA membrane group (the decreasing rate of MCP-1 in PS or CTA membrane group vs. AN69 membrane group; -35.31 +/- 18.27 % vs. -43.89 +/- 15.74%; respectively; p<0.05 ). In addition, the FMD% in AN69 membrane group were significantly higher than those of PS or CTA membrane group after hemodialysis (FMD% 6.42 +/- 2.92 % vs. 4.14 +/- 1.16 % respectively; p<0.05 ). However, we could not find any significant change on PWV between PS or CTA membrane group and AN69 membrane group. **CONCLUSIONS:** These findings suggested that the AN69 membrane improved endothelial functions by decreasing the level of MCP-1 after hemodialysis and the improvement may lead to alter the clinical symptoms which relate to peripheral circulation on hemodialysis patients.

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## **71. Regional Citrate Anticoagulation Limits Sepsis-Associated Tissue Injury Through The Decreased Release Of Microvesicles From Activated Leukocytes And Platelets**

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<sup>1</sup>Nephrology, Dialysis and Kidney Transplantation Unit, University of Turin, Italy, <sup>2</sup>Nephrology and Dialysis Unit, Cuneo Hospital Italy, <sup>3</sup>Fresenius Medical Care, Bad Homburg, Germany

Recent studies suggested that during extracorporeal blood purification for sepsis, regional citrate anticoagulation (RCA) inhibited the inflammatory response and decreased mortality. Microvesicles (MVs) are small particles released by activated leukocytes and platelets potentially involved in tissue injury in association with inflammatory cytokines. The aims of this study were: 1) to characterize MVs from plasma of septic patients and to correlate their concentration with outcome; 2) to define a potential role of MVs in the mechanisms of sepsis-associated acute kidney injury (AKI) and immunoparalysis; 3) to evaluate the role of RCA in the inhibition of MV-mediated cellular damage.

Plasma samples were collected from septic patients (n=20) to analyze MVs (FACS, Nanosight and RNA profiling). RIFLE/SOFA scores were calculated. CVVH or CVVHD with heparin or citrate (CiCa Multifiltrate, Fresenius Medical Care) were performed. In vitro, whole blood or separated leukocytes and platelets were activated by LPS and cytokines in presence or absence of citrate to evaluate MV release. The effects of septic plasma MVs were evaluated on human kidney-derived endothelial and tubular epithelial cells or lymphocytes.

Plasma MV concentration was higher in septic than healthy subjects and correlated with severity of illness and mortality. MVs from septic patients were immunologically active (class I and II HLA antigens) and expressed proteins (Fas-L/CD40-L)

and different subsets of mRNAs and microRNAs involved in inflammation and apoptosis. Plasma MVs were internalized in lymphocytes, kidney-derived endothelial and tubular epithelial cells inducing functional alterations and apoptosis. RCA but not heparin anticoagulation was associated with lower levels of circulating MVs. Similar findings were observed in vitro during CVVH or CVVHD with LPS-activated blood. Citrate significantly reduced the release of MVs from leukocytes and platelets activated by LPS. Last, MVs released from cells incubated with citrate showed a significant reduction of their ability to induce apoptosis.

In conclusion, during sepsis MVs are released by activated leukocytes and platelets in correlation with severity of illness and mortality. MVs play a potential role in the pathogenetic mechanisms of AKI and immunoparalysis. RCA may exert a protective effect by blocking intracellular calcium essential for MV release, thus limiting inflammation, mitochondrial dysfunction and apoptotic cell death.

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## **72. Outcome in Patients with Acute Renal Failure after Trauma When Continuous Renal Replacement Therapy is Applied Early vs. Late**

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<sup>1</sup>*Ajou university of hospital, Suwon, Gyeonggi-do, Korea*

**Purpose:** This study's aim is to determine whether the timing of start of continuous renal replacement therapy (CRRT) affects mortality in patients with ARF after severe trauma, and whether early start of CRRT affects restoration of damaged kidney function.

**Methods:** We reviewed the electronic medical records of 65 severe trauma patients who underwent a CRRT from January 2009 to November 2012. We compared survival, length of stay in ICU, length of stay in hospital and duration of renal replacement period between early starter and late starter groups stratified by blood urea nitrogen, urine output and RIFLE criteria.

**Results:** There is any differences between early starter group and late start group in sex, age, mechanism of injury, Injury severity score (ISS) and transfusion amount in 48 hours from ER visit. Total survival rate was 29.23% (19/65) and 30-day survival rate after initiating CRRT was 43.08% (28/65). In survivor, the patients who can live without renal replacement therapy was 84.21% (16/19) and two patients should keep conventional hemodialysis therapy. There is no significant difference between two groups about mortality ( $p=0.167$ ).

**Conclusion:** The patients who require CRRT after trauma have a high mortality rate. And initiation of CRRT, stratified into early starter and late starter by BUN and RIFLE, showed no significant difference in mortality.



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## **73. Relationship of Cystatin C with Cardiovascular risk factors and Inflammatory markers in Hemodialysis**

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<sup>1</sup>*CHA University, Seongnam, Gyeonggi, South Korea*

**Background :** Cystatin C was reported as a predictive factor for cardiovascular disease in chronic kidney disease (CKD) patients. In a study for non-dialysis CKD patients, cardio-ankle pulse wave velocity (ca-PWV) is significant related with cystatin C and in other studies for general population or non-dialysis CKD patients, it was reported that cystatin C is a significant predictive factor for cardiovascular (CV) risk irrespective of glomerular filtration rate. The purpose of this study was to evaluate the relationship of serum cystatin C with CV risk factors, inflammatory marker in the HD patients.

**Methods :** This study is a cross sectional study and we enrolled 45 HD patients. We measured CRP, TNF-alpha, IL-6, urea reduction rate (URR), lipid profile, insulin and glucose before HD, pre- and post-HD cystatin C. The ca-PWV reflecting for the degree of atherosclerosis was performed within 1 month. By the assessment of these laboratory data and review of medical records, we calculated Framingham risk score for cardiovascular disease and homeostasis model assessment-estimated insulin resistance (HOMA-IR). We measured the serum pre- and post-HD cystatin C after 1 month, and categorized

three groups by measuring the average with initial value.

Results : the average of cystatin C before HD was  $6.57 \pm 1.02$  mg/L, and we categorized three groups by Low ( $<6.49$  mg/L; n=18), intermediate ( $\geq 6.49$  mg/L,  $<7.41$  mg/L; n=18), high ( $\geq 7.41$  mg/L; n=9) according to cystatin C level. In these groups, there is no difference in age, body mass index (BMI), lipid profile, PWV, inflammatory factor, Framingham risk score and HOMA-IR. In relationship between serum cystatin C and CV risk factor, there was not associated with PW, IL-6, TNF- $\alpha$ , CRP, Framingham risk score and HOMA-IR. In assessment of the relationship between in vivo production of cystatin C and CV risk factor, there was not significant associated with the difference in pre- and post-HD cystatin C. There was significant correlation between pre- and post-HD cystatin C (coefficient=0.319,  $p=0.014$ ) and this value has strong correlation after correction of difference in dialysis membrane. (coefficient=0.596,  $p<0.001$ ). It assumes that dialysis membrane affect the concentration of cystatin C after HD. There is not significant correlation with URR and cystatin C reduction rate ( $p=0.221$ ). Conclusion : the serum cystatin C was not associated with traditional CV risk factor and inflammatory factors in HD patients.



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#### **74. A Pilot Study Aimed To Evaluate The Loss Of Carnitine During Intermittent (IHF) and Continuous Veno-Venous Hemofiltration (CVVH) In Acute Kidney Injury (AKI) Patients**

Alfonso Pacitti<sup>1</sup>, Paola Inguaggiato<sup>1</sup>, Tiziana Papalia<sup>1</sup>, Guido Martina<sup>2</sup>, Vincenzo Cantaluppi<sup>3</sup>

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Background and aim of the study: Several studies reported that Carnitine species (CA) are subjected to a substantial loss during hemodialysis (HD), thus requiring a scheduled replacement. However, no data are available on CA loss induced by CVVH in AKI patients. L-CA, a small molecular weight solute unbound to plasma proteins, is mainly eliminated by a renal clearance of 1-3 mL/min, indicating an extensive (98-99%) tubular reabsorption. Basing on the rate of artificial clearance, during CVVH a loss of CA should be estimated  $>10$  times greater than normal. The aim of the study was to evaluate the depurative kinetic of different CA species during post-dilutional (PD) IHF and CVVH.

Methods: CA species (Laevo-, Acetyl-L- and Propionyl-L-carnitine) were dosed by chromatographic methods in 5 AKI patients submitted to PD CVVH and in 5 CKD patients treated by a single PD IHF session. CA plasma values (CAs) were corrected for Plasma Water (PW) exclusion, to compute the Sieving Coefficient (SC) by the ratio of CA effluent (EF) (CAEF) to CA PW (CAPW) concentrations. In another group of AKI patients (n=5), L-CA levels were measured daily during CVVH treatment. In CKD patients, CAEF were measured on total EF collection.

Results: In AKI as well as CKD patients, the mean SC values of every CA species were into the lower limit of confidence of 1.0 ( $p<0.01$ ), indicating the identity among CAPW and CAEF and a complete passage through the membrane. In the AKI group on CRRT, the plasma CAs significantly decreased from  $26.88 \pm 2.4$  to  $6.95 \pm 2.6$   $\mu$ M/L in a period of  $14.4 \pm 1.8$  days. In CKD patients on IHF, a decrease of CA during the session was observed with a rebound at 30' after the end (slower equilibration of inner body compartments). The total loss of CA species measured on EF collection was proportional to CA income and CAs: the only CKD patient in treatment with L-CA (1g i.v. 3 times/week) had a loss of  $583 \pm 29$  mg compared to the average value of  $52.6 \pm 14$  of the other cases.

Conclusions: Prolonged intense CVVH treatment was associated with a daily loss of hundred of milligrams of L-CA. The SC observed in PD CVVH and confirmed in PD IHF suggested that CA was efficiently removed by convection-based techniques. CA loss could be hardly compensated by endogenous synthesis for the slow subtraction and the substantial equilibration of the body compartments. The depletion of CA body pool during CVVH may be a co-factor for critical illness neuro/miopathy and organ dysfunction.

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## **75. Acute Kidney Injury and Fluid Overload During Pediatric Extracorporeal Membrane Oxygenation are Associated with Increased Mortality: a Report of the Multi-centre KIDMO Study Group**

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**Background:** Extracorporeal membrane oxygenation (ECMO) is a life-saving therapy for children with severe cardiac and/or respiratory failure. ECMO patients are at increased risk of acute kidney injury (AKI), fluid overload (FO) and a need for renal support therapy. Current literature on AKI and FO in ECMO patients mainly consists of single center experiences with small patient numbers. We aim to evaluate in a multi-center study the incidence and impact on outcomes of AKI and FO in children on ECMO.

**Design/Methods:** We present a preliminary analysis from an ongoing retrospective review of children at 4 centers from the Kidney Interventions During Membrane Oxygenation (KIDMO) study group receiving ECMO from 2007-2011. AKI was defined based on the creatinine criteria of the Kidney Disease: Improving Global Outcomes guidelines. FO was calculated at the initiation of ECMO and during ECMO by cumulative ins/outs. Children with incomplete data were excluded. Outcomes included ECMO mortality and in-hospital mortality.

**Results:** 358 of 392 patients had adequate data for analysis. ECMO mortality was 24.0% and in hospital mortality was 39.7%. AKI was present in 18.1% (N=64) of children at ECMO initiation (stage I=9, II=18, and III=37). Overall, AKI was present in 47.8% (N=171) of children during the course of ECMO (stage I=19, II=23, and III=129). AKI during the course of ECMO was associated with increased ECMO mortality (36.3vs12.8%,  $p<0.001$ ) and increased in-hospital mortality (53.2vs27.3%,  $p<0.001$ ). The degree of FO at ECMO initiation was not significantly different between ECMO survivors and non-survivors (12.2% vs. 15.7%,  $p=0.15$ ), but was significantly lower in hospital survivors vs. non-survivors (11.3% vs. 15.6%,  $p=0.045$ ). Peak FO during ECMO was lower in ECMO survivors vs. non-survivors (34.8% vs. 57.8%,  $p<0.001$ ). Similarly peak FO during ECMO was lower in hospital survivors vs. non-survivors (30.6% vs. 55.0%,  $p<0.001$ ).

**Conclusions:** In this multi-centre report we found that AKI is more common during ECMO than previously reported by the Extracorporeal Life Support Organization registry. There is a strong association between AKI and mortality. Severe FO commonly occurs during ECMO and is associated with increased mortality in this cohort. Further analysis which will incorporate data from 2 additional centers is planned to further delineate the association between AKI, renal support therapy, FO on survival and other important clinical outcomes.



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## NURSING ISSUES

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### 76. Eleven Key Areas of Renal Nurse Responsibility - The Foundations of Quality Patient Dialysis Outcomes

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#### Background

Renal nurses develop their expertise over time and in the exercise of their professional skills deliver the essence of safe, competent, and compassionate care. Across Saudi Arabia, there is an absence of nursing core competencies of a renal nurse apart from other nurse practitioners.

#### Objective

This study identifies whether Quality Patient Dialysis Outcomes (QPDO) were directly affected by eleven key areas of nurse responsibility used when evaluating renal staff competency (SC).

#### Methods

59 Staff Nurses were appraised evaluating SC while 525 hemodialysis patients were evaluated using the QPDO parameters. Univariate linear regression and Pearson rho moment correlation were used to build relationships.

#### Results

Data indicated both increase and decrease trends in relation to staff competency. Competencies related to Health Education (↑172.6), Communication (↑147.5), Records Management (↑141.6), Safe and Quality Nursing Care (↑135.0), and Management of Resources (↑133.5) demonstrated increase trends. Competencies related to Research (↑-35.2), Quality Improvement (↑-12.3), and Legal Responsibility (↑-6.68) were relatively decreased as the period of competency evaluation progressed. It was notable that QPDO related to Kt/V, Albumin, Hemoglobin, and Hematocrit Levels were directly proportional to increasing extent of SC  $\rho$ =(+0.61) while calcium and phosphorus levels were directly associated to areas where staff were demonstrated an decreasing trend  $\rho$ =(+0.66).

#### Conclusion & Implication to Practice

The eleven key areas of responsibility used to measure SC in a periodic evaluation demonstrated a strong correlation to the increasing extent of QPDO. Additionally, as the nurses progressed to becoming expert a direct correlation to the QPDO was notable. The study became the foundation for staff training and developing a competency appraisal framework in renal nursing practice thereby promoting quality assurance procedures while attaining QPDO.

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### 77. Enhancing Safe Administration of Anticoagulation Therapy in Saudi Arabia – A Challenge in Nursing practice

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#### Background:

Effective heparinization during dialysis is vital since it allows blood to flow into the extracorporeal circuit.

#### Objective:

This study aimed to develop a relationship between errors in Heparin administration and the study of Partial Thromboplastin Time (PTT), Hemoglobin (Hgb), Hematocrit (Hct), and Platelet levels (Plt) of hemodialysis (HD) patients.

#### Methods:

255 HD patient records were examined for compliance and errors in heparin administration practices. With multiple tendencies, cox regression was used to analyze trends whilst Pearson rho moment correlation determined relationships.

#### Results

The results indicated that heparin was administered via three routes namely bolus (90.47%), maintenance (100% via machine, 19.04% via manual approach), and preparation and administration. It was significant that only 8% of nurses followed the Independent Double Check method of heparin preparation and administration which was a required standard within the unit. Data showing both medication administration practices and extent of errors versus the mean scores of the PTT, Hct, Hgb and Plt were analyzed individually showing a significant regression of PTT ( $r=1.38, 1.50$ ), Hgb ( $r=0.80, 1.03$ ), Hct ( $r=1.11, 1.07$ ), and Plt ( $r=1.22, 1.27$ ). Results were summed and revealed strong correlation between the errors versus the mean values of the PTT ( $p=+0.77$ ), Hct ( $p=0.55$ ), Plt ( $p=+0.67$ ) with the exception of Hgb which did not show any correlation at all  $p=+0.04$ .

#### Conclusion AND Application to Practice:

The results of this study led to the development of a standardized protocol minimizing errors relating to heparin administration during dialysis. Additionally, the study provided a Process Map when untoward incidences relating to use of Low Molecular Weight Heparins occurred. Further, the study has led to a significant decline in errors in medication administration practices in general within the unit.

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### 78. Innovations in CRRT Training: Leveraging simulation for a multidisciplinary CRRT Symposium.

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Purpose: Describe the use of simulation-based training to enhance CRRT learning.

#### Background:

CRRT use is limited by lack of understanding of its application and technical features. A 2-day seminar limited to 50 participants used simulation-based training to increase understanding of CRRT for physicians, pharmacists, and nurses.

#### Methods:

Day 1 used a didactic format on CRRT basics. On day 2, participants were divided into Nursing and Physician/Pharmacy/Advanced Practice (AP) groups. Each group was subdivided into smaller groups, permitting small faculty-to-participant learning ratios (1:5-6) for simulation-based sessions.

Breakout sessions utilized the UAB simulation center and a variety of teaching methods including small group discussion, hands-on problem solving with machine simulations, and case studies for lab interpretation and management. Some breakouts used high fidelity simulation mannequins with CRRT machines circulating simulated blood. Five breakouts were designated for nursing; 5 for physician/AP. Groups rotated through each of their designated stations. Nursing breakouts included an overview of fluid and electrolytes, implementation of physician orders, machine set up and troubleshooting, CRRT labs, and a synthesis station. Physician/AP breakouts focused on patient selection, order sets, troubleshooting electrolytes, and life-like case simulations on anticoagulation and CRRT dose.

Afterwards, all participants regrouped for a session on ethics and palliative care. They then viewed a 6-part series of interrelated video vignettes of simulated interactions of the multidisciplinary team, patient and family. Topics such as consent, troubleshooting, managing family expectations, and termination of CRRT were highlighted. Each vignette was followed by a facilitated debriefing that encouraged experiential learning and open discussion with consideration of each discipline's unique perspectives and needs.

#### Results:

Evaluations included an overall evaluation, simulation evaluations, and individual session evaluations. The mean score was 4.92/5.0. Comments included: "I feel better prepared to care for CRRT patients"; and simulations allowed "me to understand the classroom content better," "assimilation of lecture theory into practice," and "time for questions and clarifications."

#### Conclusion:

The innovative multidisciplinary curriculum enhanced retention and application of CRRT by using simulation-based teaching strategies.

## 79. How to make a Quick Change of CRRT Machines

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How to make a quick change of CRRT machines

We had to make a change from Aquarius to NxStage

We are a multidisciplinary unit with 11 beds; our patients are surgical and medical

We treat approximately 75 -90 patients per year.

In a group of 70 nurses, who all receive training in CRRT, a quick change is a challenge.

However, we made the change over a period of 3 weeks, and even though there were problems, they were minor, and the staff's skills were maintained.

In relation to the change of machines, we made a greater change in our treatments, and we changed modes and fluid rates.

We want to show our program, and explain the importance of the staff's understanding of the change.

Our staff is trained in a 3 step program towards a high level of competence in CRRT, and at completion of the training they get a monthly bonus.

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## 80. Continuous Renal Replacement Therapy Education to Improve Parental Understanding and Satisfaction

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Initiation of pediatric continuous renal replacement therapy (CRRT) for a critically ill child represents an escalation in level of care that may be anxiety provoking for families. Despite a detailed procedural explanation performed by a nephrologist before initiating CRRT, there is no currently available means by which to measure basic parental/guardian understanding and comfort level pertaining to performance of CRRT. Additionally, while there is literature describing means by which to educate members of the hospital care team, no published literature exists demonstrating an approach to educating families about CRRT. We have developed an informational handout in both English and Spanish to be given to the families of our patients who are treated with CRRT. Complementing the patient education material is a guide for nurses educating the family. We hypothesize that provision of this handout will help alleviate anxiety – especially those associated with alarms/display panels/lines - and increase understanding of provision of CRRT to a child with acute kidney injury (AKI). To determine the effectiveness of supplying this additional information to families, we plan to proceed with our usual standard of care to each patient, which includes a detailed procedural explanation performed by a nephrologist/fellow before initiating CRRT when consent is obtained. For patients less than 18 years age, our study team will approach the family to obtain consent for participation, after which a family member will complete a brief Likert scale-based survey to determine their basic understanding of AKI, the CRRT procedure, medical team members involved, and comfort level with the procedure. Upon completion of the survey, the study team will provide the family with our informational handout. Laminated copies of the handout will be attached to the CRRT machine and maintained in the patient's room for others to view as well. 24-48 hours after the handout is introduced, the family member will be re-surveyed to determine if the handout helped provide informative information. We plan to enroll 20 patient families, analyze our results, including determination of mean scores for each survey point, assessing for pre- and post-intervention significance ( $p < 0.05$ ).

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## 81. Implementation of CRRT in a Community Hospital Setting in Partnership with a Contracted Dialysis Service

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**Purpose:** Acute Kidney Injury (AKI) in the ICU has been shown to significantly contribute to increased mortality and morbidity (Brochard, et al 2010). Continuous renal replacement therapy is a complex modality that is usually reserved for the large tertiary care facilities as it is costly and requires 24 hour surveillance and troubleshooting.

**Setting:** Methodist Willowbrook Hospital is a 251 bed acute hospital located in Houston, Texas. Critical Care consists of a 16 bed Surgical ICU and a 16 bed Cardiovascular ICU. Dialysis services are outsourced to Davita Hospital Services Acutes. At the request of the physicians, the hospital was asked to provide CRRT services. Due to the high risk and low frequency of this service, the Director of Nursing decided to seek partnership with Davita Hospital Services Acutes to support the implementation of these services.

**Participants/Subjects:** All patients admitted to Critical Care Services who required CRRT as deemed by a nephrologist/critical care physician

**Methods:** The Director of Critical Care Services met with the Davita Regional Director in the fall of 2010 to formulate a model for implementation. Davita agreed to purchase the capital equipment needed and train the ICU staff for initial implementation and ongoing continuous education. The Director of Nursing felt that the ICU nurses would need assistance with the following:

1. Setting up the CRRT upon initiation
2. Troubleshooting alarms
3. A daily round to ensure machine is working properly and fluid removal is correct
4. Discontinuing CRRT

The ICU nurses could be trained to manage ongoing maintenance to include adjusting flow rates, managing anti-coagulation and recording fluid volumes. A contract was negotiated and the plan was placed into action. The contract included the following items: Initiation of CRRT, daily round charge, and cancellation set up.

The plan was placed into policy and approved for implementation. In addition order sets and documentation flow sheets were developed with the assistance of Davita. The pharmacy director was notified of this new service. The nephrologists were in support of this program as well. In concert with Davita and the CRRT machine vendor, approximately 10 ICU nurses were trained in the Spring of 2011. The first patient was initially placed on CRRT in the early summer of 2011 without incident.

References upon request

CRRT Economic Outcomes	2011-2012
Current Volume	3 patients per month
Capital Cost Savings	Approx. 70 K
Cost of Supplies Savings per year	Approx. 24 K based on current volume