CRRT 2014

NINETEENTH INTERNATIONAL CONFERENCE ON CONTINUOUS RENAL REPLACEMENT THERAPIES

MARCH 4-7, 2014 MANCHESTER GRAND HYATT SAN DIEGO, CALIFORNIA

SPECIAL SESSIONS - ORAL PRESENTATIONS

Tuesday March 4, 6:00-7:30pm

Session A
EPI and Outcomes

Co-Chairs:
Patrick Murray and
Josee Bouchard

11. Braun, Andrea*
15. Botdorf, Joshua*
27. Balderas Juarez, J*
5. Venegas Justiniano, J*
6. Schetz, Miet
13. Patil, Neha
7. Schetz. Miet
22. Powell, T Clark
16. Sileanu, Florentina
12. Askenazi, David

* denotes Fellow

Session B
Basic Research in AKI

Co-Chairs:
Samir Parikh and
Roland Blantz

36. Peng, Zhiyong
34. Pottumarthi, Prasad
37. Gomez, Hernando
52. Cantaluppi, Vincenzo
38. Askenazi, David
45. Wen, Xiaoyan
48. van Elsas, Andrea
44. Wen, Xiaoyan
49. Won Min, Hwang
77. Zhang, Jicheng

Session C
RRT Technique Characteristics and RRT Targeted Applications

Co-Chairs:
Marlies Ostermann and Kianoush Kashani

53. Walther, Carl*
57. Grover, Vanya*
58. Chebib, Fouad
56. Zanella, Monica
60. Iacovella, Gina*
63. Carlsson, Ola
64. Saxena, Anil
65. Vega, Molly
66. Vincenzo. Cantaluppi
84. Guru, Pramod

Wednesday March 5, 6:00-7:30pm

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EPI and Outcomes

Co-Chairs:
Emmanuel Burdmann and
Sean Bagshaw

18. Bransi, Myriam
20. Maccariello, Elizabeth
24. Sevag, Demirjian
17. Li, Zhang
28. Vazquez-Rangel, Armando
26. Quercia, Alessandro
23. Powell, T Clark
8. Wijewickrama, Eranga
21. Rege, Tanvi
25. De La Garza, Keila

Session B
Clinical Research in AKI

Co-Chairs:
Michael Joannidis and
Chirag Parikh

33. Cheungpasitporn, Wisit*
42. Kaddourah, Ahmad*
43. Parr, Sharidan*
29. Solomon, Richard
40. Zarbock, Alexander
46. Goldstein, Stuart
51. Neyra, Javier*
32. Akrawinthawong, Krittapoom*
47. Yamashita, Tetsushi*
71. Stevenson, Emma*

Session C
New Technology RRT Research & Nursing Issues

Co-Chairs:
Ian Baldwin
Luis Juncos

73. Parekkadan, Biju
72. Oh, Joon Seok
69. Garzotto, Francesco
68. Ludes, Scott
30. Sakai, Masahito*
79. Lewis, Susan*
83. Murugan, Raghavan
85. McCarthy, Paul
86. Benfield . C Brett (NAP)
89. McMillan, Cynthia (NAP)

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Nursing Issues

Abstract Number 3

Morbidity and Mortality Multicenter Behavior of Acute Kidney Injury. Two Decades Follow-up

Nadienka Rodríguez Ramos[1], Lietny M Becerra Castillo[1], Leonel Soto León[1]

[1]*Abel Santamaria Hospital*

With the purpose of describing the clinical behavior of Acute Kidney injury; the morbidity and mortality of this syndrome and the detection of the aspects that are susceptible to modification to accomplish an improvement on the evolution and prognosis of these patients, was performed an analytical and longitudinal multicentre study in the western area of Cuba, in 1567 patients with age older than 19 years, classified by suffering of acute kidney injury with need of dialysis on the period of January 1992 to December 2012. Was used a data collecting card with information obtained from the review of the patient's medical record, were assessed the clinical, humoral and prognosis variables. Were used summary measures, OR ratio and Chi-square 0,95% for $p < 0,05$. The data was displayed on tables and graphics. The masculine sex prevailed, and the 25 – 59 age groups on both sexes in which the early diagnosis based on AKIN criteria improved a great deal the prognosis. The APACHE II was directly and proportionally associated with the presence of AKI and with its mortality. The patients with oliguric AKI have a greater possibility of dying, situation that is reduced on the ones that received treatment with hemodialysis which affected positively on a better prognosis, therefore it can be considered as a protective factor.

Abstract Number 4

Acute Kidney Injury According to "RIFLE" Criteria on Patients Admitted in Intensive Care Unit.

Nadienka Rodríguez Ramos[1], Loreile González Mazón[1], Zenaida Hernández Boza[1]

[1]*Abel Santamaria Hospital*

To diagnose the Acute Kidney Injury on patients admitted in intensive care at the Abel Santamaría Hospital during the years 2011-2012, was developed an observational, descriptive and retrospective study; the sample consisted of 768 patients that complied with the inclusion criteria. The patients were classified according to RIFLE to diagnose Acute Kidney Injury. The obtained data was processed with absolute and relative frequencies, which were displayed on tables and graphics. The quantitative results were condensed using central tendency and was calculated the homogeneity between groups using the standard and corrected Chi-square test according to Yates. Obtaining that almost half of the patients developed different levels of Acute Kidney Injury and prevailed on those which the admission cause was surgical, proving that age and heart failure are the more frequent risk factors; in addition to sepsis as the greater precipitant factor and the contraction state of the intravascular liquid, respectively. The RIFLE classification proved to be an important prognosis tool for the association between its highest levels with mortality. Creatinine was one of the more used parameters for the diagnosis of Acute Kidney Injury and, with higher severity of AKI, higher will be the need for kidney replacement therapy, and higher will be the mortality and smaller the possibility of kidney function recuperation.

Abstract Number 5

"Clinical and Epidemiological features in patients with Acute Kidney Injury in a Critical Care Unit in Lima-Peru"

YANISSA Y VENEGAS[1], ABDIAS HURTADO[1]

[1]*UNIVERSIDAD PERUANA CAYETANO HEREDIA/HOSPITAL NACIONAL ARZOBISPO LOAYZA*

Objective: To describe the clinical and epidemiological features among patients with acute kidney injury (AKI) - stage 3 AKIN, in the critical care unit at "Arzobispo Loayza National Hospital" (HNAL), Lima- Peru. January - June 2013.
Materials and Methods: A retrospective, cross sectional study was performed. We evaluated 40 clinical records of patients who developed AKI stage 3 during their ICU stay and who met the inclusion criteria.
Results: The frequency of AKI in ICU was 15,8% and the mortality rate was 42,5%. The causes for admission to ICU were: circulatory failure (100%) and respiratory failure (85%). Septic shock was the most common cause for circulatory failure. 23 (57,5%) patients survived and 17 (42,5%) died. The mean age was 54,7 ± 17,4 years and 60% were men. Among patients who died, oliguria, low pH and platelets, hyperkalemia, high anion gap, total bilirubin, APACHE, SOFA and Liaño scores, were statistically significant. In the logistic regression: oliguria and elevated anion gap were factors associated with mortality. Survival at 14 and 30 days was 55 and 41% respectively.
Conclusions: AKI in ICU is a common condition with high mortality. The most important factors associated with mortality were high anion gap and oliguria.
Keywords: Acute renal injury, stage 3 AKIN, critical care unit, morbidity, mortality

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Abstract Number 6

eGFR versus Creatinine Clearance for Evaluation of Recovery from AKI

Philippe Timmermans[1], Jan Gunst[1], Greet Vandenberghe[1], Miet Schetz[1]

[1]*KULeuven - Department of Intensive Care Medicine*

Introduction

Recovery of AKI is frequently evaluated by comparing discharge serum creatinine (Screat) or estimated GFR (eGFR) with baseline Screat or eGFR. However, the relationship between Screat and GFR may change significantly during ICU stay, especially in patients with prolonged ICU stay and muscle wasting. The aim of this study is to quantify the impact of using eGFR instead of measured creatinine clearance (Clcr) on the estimation of renal recovery.

Methods

In a large database (n=4560) of a heterogeneous ICU population 1296 patients developed AKI according to the KDIGO criteria. After exclusion of ICU non-survivors (n=229), patients on dialysis at ICU discharge (n=77) and patients for whom Clcr on the last day of ICU was not available (n=206), 784 patients were included in this analysis. We compared eGFR (MDRD equation) with measured Clcr (based on 24h urine collection and corrected for BSA) at ICU discharge for patient groups with different ICU stays. We also evaluated the impact of using the two GFR measurements on the estimation of complete recovery relative to baseline eGFR. Parameters were compared with the paired t-test and McNemar's test.

Results

Amongst the 784 patients with AKI, 456 (58%) reached stage 1, 143 (18%) stage 2 and 185 (24%) stage 3. Mean±SD Clcr at ICU discharge was 54,5±28 and eGFR was 76±55 ml/min/1.73m2 ($p<0.0001$). When patients were divided according to their ICU stay, eGFR was not significantly different from Clcr in patients with ICU stay below 7 days. In patients with ICU stay between 8 and 14 days the difference became highly significant and increased even further in patients with ICU stay over 14days (see Table). Also the percentage of patients with complete recovery differed significantly when evaluated by eGFR (35.3%) or Clcr (28.7%) (p0.007). In patients with ICU stay above 14 days, this difference increased to 56.4% by eGFR versus

14.1% by Clcr (p<0.0001).

Conclusion

Estimated GFR at ICU discharge is significantly higher than measured Clcr in patients with prolonged ICU stay. This difference can be explained by loss of muscle mass with decreased creatinine production and results in an important overestimation of recovery.

ICU stay	n	Clcreat	eGFR	P	Mean diff	complete recovery by Clcr	complete recovery by eGFR	p
		mean +/- SD	mean +/- SD		(95% CI)	(%)	n (%)	
All	784	54.5 ±28	76 ±55	<0.0001	21.6 (17/26.2)	225 (28.7)	277 (35.3)	0.007
ICU 1-7d	399	64 ±31	60±36	0.13	-3.7 (-8.7 / 1.2)	160 (40)	76 (19)	<0.0001
ICU 8-14d	158	48.5 ±20	79 ±51	<0.0001	30.9 (22.4/39.3)	33 (21)	73 (46.2)	<0.0001
ICU >14d	227	42.6 ±20	102 ±70	<0.0001	59.7 (49.8/69.6)	32 (14.1)	128 (56.4)	<0.0001

Abstract Number 7

Recovery from AKI Assessed by KDIGO Criteria.

Dominique Schrijvers[1], Jan Gunst[1], Greet Vandenberghe[1], Miet Schetz[1]

[1]*KULeuven - Department of Intensive Care Medicine*

Introduction

Data on recovery of AKI is mainly limited to persistent dialysis-dependency in patients with dialysis-requiring AKI, whereas results on recovery from less severe forms of AKI are scarce.

Methods

In a large database (n=4560) of a previous RCT including a heterogeneous population of ICU patients we estimated renal recovery from different stages of AKI defined by KDIGO criteria (without urine output criteria). Patients were classified according to their maximal AKI stage (AKImax) during ICU stay. Recovery was evaluated by AKI stage at hospital discharge. Complete recovery was defined as the absence of AKI, partial recovery as persistent AKI with a decrease in AKI stage compared with AKImax and no recovery as persistence of AKImax or worsening of AKI after ICU discharge. A persistent 0,3mg/dL increase of Screat was also considered as no or partial recovery.

Results

1296 patients (28%) developed AKI. AKImax was stage 1 in 580 (45%)(416 with >50% increase of Screat), stage 2 in 207 (16%) and stage 3 in 509 (39%) (348 needing RRT). Hospital mortality, ICU and hospital stay and kidney recovery are shown in table 1. Mortality increased from 12 to 42% (p<0.0001) and complete recovery in survivors decreased from 82 to 53% (p<0.0001) with increasing severity of AKI. In patients requiring RRT 61% of survivors left the hospital without AKI, whereas 16% remained dialysis-dependent. Within the AKI 3 group, the need for RRT significantly increased mortality (p0.0002), but did not affect complete recovery in survivors (p0.16). Patients with a “0.3mg/dL increase of serum creatinine only” had a significantly higher mortality than patients without AKI in ICU (p0.0004). They also had a worse kidney outcome at hospital discharge (p0.006).
continued

Conclusion

Increasing severity of AKI according to the KDIGO criteria is associated with increased mortality and decreased recovery of kidney function, with complete recovery in survivors varying between 82 and 53%. The need for RRT significantly increases mortality but complete recovery in survivors of AKI 3 is not different with or without RRT. The 0.3mg/dL criterion is associated with mortality and worse kidney outcome.

AKI max (ICU)	Incidence	Mortality	ICU stay	Hospital stay	Complete recovery in survivors	Partial recovery in survivors	no recovery or worsening in survivors
	n (%)	n (%)	median (IQR)	median (IQR)	n (%)	n (%)	n (%)
no AKI	3264 (71.5)	136 (4.1)	5 (2-11)	13 (9-21)			129 (4.1)
AKI stage 1	580 (12.7)	70 (12.1)	6 (3-11)	21 (14-37)	419 (82)	29 (6)	62(12)
stage 1 - "0.3 only"	164 (3.6)	18 (11)	6 (3-11)	19 (14-33)	132 (90.4)		14 (9.6)
stage 1 - 50% incr	416 (9.1)	52 (12.5)	6 (3-11)	22 (14-38)	287 (78.8)	29 (8%)	48 (13.2)
AKI stage 2	207 (4.5)	44 (21.2)	9 (5-18)	28 (15-46)	115 (70.5)	41 (25)	7 (4)
AKI stage 3	509 (11)	216 (42.4)	16 (8-31)	34 (17-63)	157 (53.5)	101 (34.5)	35 (12)
stage 3 no RRT	161 (3.5%)	49 (30.4)	9 (6-14.5)	26 (14-47)	65 (58)	44 (39)	3 (2.7)
stage 3 + RRT	348 (7.5)	167 (48)	21 (12-37)	39 (20-67)	92 (51)	57 (31)	32 (18)
p for stage effect		<0.0001	<0.0001	<0.0001	<0.0001		

Abstract Number 8

Acute Kidney Injury in a Medical Intensive Care Setting; Single Unit Experience

Eranga S Wijewickrama[1], Gowri M Ratnayake[2], Chaminda Wickramaratne[2], Rezvi Sheriff[1], Senaka Rajapakse[1]

[1]Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Colombo, Sri Lanka, [2]National Hospital of Sri Lanka, Colombo, Sri Lanka

Introduction:
Acute kidney injury (AKI) is a common and a serious complication among patients admitted to intensive care units (ICUs) and has been the focus of many studies leading to recent advances in diagnosis and classification. The incidence and outcome of AKI in Sri Lankan ICUs is largely unknown. The aim of this study was to describe the incidence, severity and clinical outcome of AKI among patients admitted to the medical ICU of National Hospital of Sri Lanka (NHSL).
Methods:
Patients admitted to the medical ICU, NHSL, over a period of 6 months were studied prospectively. Standard demographic, physiological and clinical data were collected. Clinical data encompassed primary diagnosis, presence of co morbidities and need for mechanical ventilation. Physiological data included Glasgow Coma Scale, arterial oxygen tension (PaO2)/fraction of inspired oxygen (FiO2) ratio, serum pH, serum sodium, potassium, bilirubin, haemoglobin, platelet and white cell count. Data on kidney function included serum creatinine, urea and urine output. Severity of illness on admission and during the ICU stay was assessed using the SOFA score.
Diagnosis of AKI was based on AKIN-criteria. Patients who had chronic kidney disease and were on renal replacement therapy, and those whose ICU stay was shorter than 48 hours were excluded. Chi-square tests and Kaplan-Meier analysis were used for comparisons.
Results:

108 patients satisfied the inclusion criteria; males 67(61.5%); mean age 47.8 (SD 19.4, range 12-94). Mean duration of ICU stay was 11.6 days (SD 10.6, range 2-55). 81(75.0%) received mechanical ventilation. 49(45.4%) had sepsis. ICU mortality was 38.9%. AKI was present in 65 (60.2%). The majority with AKI had AKI stage 3 (38, 58.5%). Thirty seven of the patients in AKI stage 3 required dialysis. Among those who received dialysis, the majority (36, 97.3%) received intermittent haemodialysis.

Patients with AKI were at higher risk of death ($p<0.01$). Neither age nor the presence of co-morbidities was associated with increased risk of AKI. Patients with AKI had significantly longer ICU stay (Log-Rank Chi Square-23.186, $p<0.0001$). Mortality rates were significantly lower among those with an initial SOFA-score<9, compared with patients with SOFA-scores>11 (30.4% vs 43.5%, Chi-Square-7.581, $p=0.006$).
Conclusion:
The incidence of AKI is high among our ICU patients, and those with AKI have a higher mortality and longer duration of ICU stay.

Abstract Number 11

Vascular Surgery Kidney Injury Prediction Score (vsKIPS): A Multivariate Derivation Cohort

Andrea B Braun[1], Daryl J Kor[1], Joshua S Botdorf[1], Gina M Iacovella[1], Pramod K Guru[1], Kianoush B Kashani[1]

[1]*Mayo Clinic, Rochester, MN, USA*

Purpose:
We developed a risk prediction model for AKI (acute kidney injury) in patients undergoing vascular surgery.

Methods:
We examined risk factors for AKI in 845 patients undergoing vascular surgery from January 2003 to May 2008 at a tertiary referral center, and then developed a multivariate model to predict AKI.
Descriptive data were summarized by medians with interquartile ranges and counts (percentages). Univariate models to predict AKI were used to identify the most significant variables to be included in the multivariate models. Stepwise backward elimination was used for variable selection in the multivariable logistic regression models. Selected predictor variables were checked for co-linearity and interactions. We used receiver operator characteristics analyses to evaluate the performance of each multivariate model. All tests were two-sided, and P values less than 0.05 were considered statistically significant.

Results:
AKI developed in 258 of 845 patients (30.5%) undergoing vascular surgery.
Compared to patients without AKI, patients with AKI had a higher baseline creatinine, lower GFR, were older, more likely to undergo emergency surgery, had hypertension, had undergone a previous vascular intervention, and received pre-operative diuretics or beta-blockers.
Variables not associated with an increased risk of AKI included gender, BMI, American Society of Anesthesiologists Physical Status, presence of congestive heart failure, diabetes, COPD, cerebrovascular disease, previous open heart surgery, smoking status, contrast exposure in the 72 hours before surgery, pre-operative use of NSAIDs, ACE-inhibitors, angiotensin receptor blockers, or statins. (see Table)
A multivariate risk prediction model that included pre-operative GFR, previous vascular intervention, pre-operative use of diuretics and beta-blockers had an area under the curve (AUC) of 0.669. A multivariate risk prediction model that additionally included the presence of emergency surgery had an AUC of 0.671.

Conclusion:
Pre-operative risk factors for AKI included a higher baseline creatinine/lower GFR, older age, emergency surgery, preexisting hypertension, previous vascular interventions, and the use of pre-operative diuretics or beta-blockers.
A risk prediction model can estimate the likelihood of postoperative AKI and facilitate risk stratification prior to surgery. Future studies are needed to evaluate the impact of changes in the modifiable risk factors.

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Variable	No AKI (n=587) (mean, standard deviation; or number of patients / percentage)	AKI (n=258) (mean, standard deviation; or number of patients / percentage)	P-value (logistic regression), significant if <0.05 (*)
Admission creatinine	1.1 +/- 0.4	1.3 +/- 0.5	<0.001*
GFR	71.8 +/- 21.3	60.3 +/- 20.8	<0.001*
Age (years)	69.5 +/- 10.0	71.4 +/- 9.5	0.012*
Gender – female / male	136 (23%) / 451 (77%)	56 (22%) / 202 (78%)	0.640
BMI (body mass index)	27.6 +/- 5.3	28.2 +/- 5.2	0.136
ASA PS 3-4	568 (97%)	251 (97%)	0.685
Emergency surgery	12 (2%)	13 (5%)	0.022*
CHF (congestive heart failure)	29 (5%)	15 (6%)	0.599
Diabetes mellitus type 1 / 2	58 (10%) / 8 (1%)	34 (13%) / 5 (2%)	0.292
Hypertension	428 (73%)	208 (81%)	0.017*
COPD	166 (28%)	75 (29%)	0.814
Cerebrovascular disease	50 (9%)	29 (11%)	0.212
Smoking status: current / former	181 (31%) / 238 (41%)	70 (27%) / 94 (36%)	0.054
Previous open heart surgery	118 (20%)	60 (23%)	0.301
Previous vascular intervention	40 (7%)	36 (14%)	0.001*
Contrast exposure within 72 hours before surgery	89 (15%)	32 (12%)	0.293
Pre-operative NSAID use	58 (10%)	28 (11%)	0.667
Pre-operative ACE/ARB use	269 (46%)	132 (51%)	0.153
Pre-operative diuretic use	202 (34%)	120 (47%)	<0.001*
Pre-operative statin use	329 (56%)	141 (55%)	0.706
Pre-operative beta-blocker use	338 (58%)	177 (69%)	0.003*

Abstract Number 12

Does Acute Kidney Injury Contribute to Bronchopulmonary Dysplasia in Very Low Birth Weight Infants?

Neha R Patil[1], Rajesh Koralkar[1], Susan Keeling[1], Namasivayam Ambalavanan[1], David J Askenazi[1]

[1]*University of Alabama at Birmingham*

Background:
Acute kidney injury (AKI) is associated with mortality in neonatal and pediatric critically ill populations. Animal and human models suggest a direct link between acute kidney injury (AKI) and acute lung injury.

Objective:
To determine the independent association between AKI and Bronchopulmonary Dysplasia (BPD) in Very Low Birth Weight (VLBW) infants.

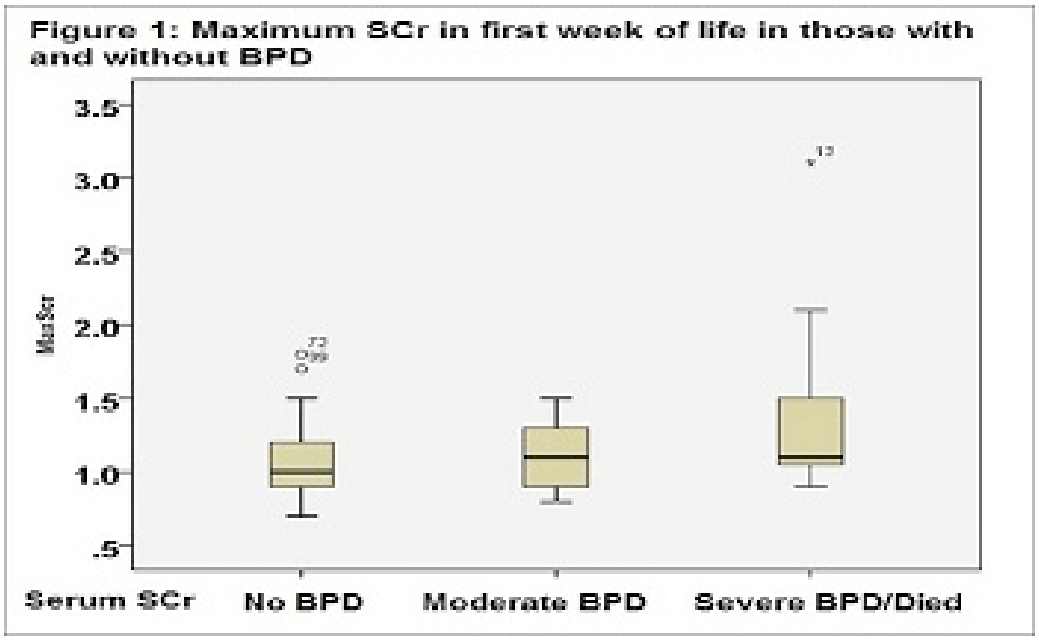
Methods:
• Study Population – 125 Consecutive VLBW Infants (birth weight <=1200 gm. or gestational age <31 weeks) were enrolled between February 2012 to February 2013.
• Definition of AKI - According to KDIGO each serum creatinine (SCr) was compared to the lowest previous value. Stage 1 AKI was defined as SCr > 0.3 mg/dl or > 150-200% from lowest previous value. Stage 2: SCr > 200-300% from lowest

previous value and Stage 3 AKI: SCr > 2.5 mg/dl or SCr > 300% from lowest previous value.
• We looked at respiratory support requirements on days 7, 14, 21, 28 and 36 week postmenstrual age (PMA) to determine differences between AKI and No AKI group. Bronchopulmonary dysplasia (BPD) was defined if an infant was oxygen dependent at 36 weeks PMA. BPD was categorized as moderate if PiO2 requirement on that day was <= 30% and severe if infant was on CPAP, SIMV or with >30% PiO2 requirement.

Results:
Cumulative incidence of AKI in our study was 30% by day 15 of life. AKI by day 3 was associated with higher respiratory support on day 14. AKI by days 7 and 15 were associated with higher respiratory support on days 7, 14, 21, and 28 and composite BPD/ mortality at 36 week PMA (Table 1). Max Scr value was higher in first week of life in those with moderate and severe BPD (Figure 1). Even after controlling for gestation age, birth weight, apgar at 1 and 5 min and preeclampsia, AKI continues to be an independent risk factor for BPD/mortality.

Conclusion:
AKI is associated with higher incidence of BPD and lower survival in VLBW infants. Even after controlling for potential confounders, AKI is independently associated with BPD/mortality. Strategies to prevent / ameliorate the impact of AKI could lead to improved BPD outcomes. Multi-center studies and animal data are greatly needed to better understand these relationships.

	AKI by Day 3		AKI by Day 7		AKI by Day 15	
BPD Status	Yes (18)	No (100)	Yes (32)	No (90)	Yes (36)	No (86)
No BPD	9 (50%)	64 (64%)	15 (47%)	62 (69%)	17 (47%)	60 (70%)
Moderate BPD	2 (11%)	8 (8%)	3 (9%)	7 (8%)	3 (8%)	7 (8%)
Severe BPD/Mortality	7 (39%)	28 (28%)	14 (44%)	21 (23%)	16 (45%)	19 (22%)
P value	0.2		0.02		0.01	



Abstract Number 13

Urine Biomarkers Predict Acute Kidney Injury (AKI) , Bronchopulmonary Dysplasia (BPD) and Mortality in Very Low Birth Weight (VLBW) Infants

David J Askenazi[1], Rajesh Koralkar[1], Russell Griffin[1], Brian Halloran[1], Neha R Patil[1], Susan Keeling[1], Namasivayam Ambalavanan[1]

[1]*University of Alabama at Birmingham*

Background:
Serum creatinine (SCr)-based AKI definitions carry important limitations, especially in neonates. Urine biomarkers improve our ability to detect organ damage and provide insight on injury/repair mechanisms. These biomarkers should not only predict a rise in SCr, but also predict hard clinical outcomes.

Objective:
To determine if 14 biomarkers measured in VLBW infants in the first 4 days of life are associated with gestational age (GA), AKI adjusted for GA, BPD adjusted for GA, and mortality adjusted for GA.

Methods:
Between February 2012 to June 2013, 116 VLBW Infants (birth weight <=1200 gm. or <31 weeks post gestational age (PGA)) were prospectively followed. SCr values were collected on days 1,2,3,4, of life and combined with clinically measured SCr to determine AKI status with modified neonatal KDIGO AKI definition (rise in SCr ≥ 0.3 mg/dl or ≥ 150-200% from baseline, which was adjusted to the lowest previous SCr to account for SCr decline after birth). BPD was defined if infants received oxygen at 36 weeks PMA. Urine was collected during the first 4 days (average number of urines obtained was 3 (range 1- 5)). Biomarker analysis was performed using the MesoScale Discovery (MSD) Human Kidney Injury Panels 3 and 5. All biomarkers samples were natural log transformed (to account for non-normal distribution) and divided by urine creatinine (Cr) (to control for concentration). Repeated measured ANOVA was performed for the log urine biomarkers/Cr and outcome of interest.

Results:
Cumulative incidence of AKI over first week of life was 28/113 (25%); 28/100 (28%) of survivors had BPD; 13/113 (12%) infants died. All urine biomarkers (except calbindin) were inversely associated with gestational age. After controlling for GA, OPN, NGAL, Clusterin, and _-GST were independently associated with AKI. After controlling for GA, _2MG, Cystatin C, NGAL, OPN, UMOD, Clusterin, KIM-1, TTF3, VEGF and _-GST were associated with BPD. After controlling for GA, _2MG, cystatin c, OPN, NGAL, Clusterin, and _-GST were independently associated with mortality (Table 1).

Conclusion:
Urine biomarkers almost uniformly are inversely associated with GA. Even after adjustment for GA we found significant associations between 5, 10 and 7 urine biomarkers for AKI, BPD and mortality, respectively. Thus, urine analysis measured on the first days of life may improve our ability to detect meaningful outcomes in VLBW infants.

table continued on followng page

	GA	AKI adjusted for GA	Mortality adjusted for GA	BPD adjusted for GA
log Albumin/Cr	-0.06 ‡	0.023	-0.09080	0.053
log B2M/Cr	-0.044 †	-0.058	0.2428 *	0.18 ‡
log CystatinC/Cr	-0.14 ‡	0.182	0.289 *	0.61 ‡
log EGF/Cr	0.024 ‡	-0.032	-0.017	-0.096 †
log NGAL/Cr	-0.16 ‡	0.205 *	0.32 *	0.53 ‡
log OPN/Cr	-0.087 ‡	0.158‡	0.25 ‡	0.32 ‡
log UMOD/Cr	0.028 ‡	-0.088	-0.10	-0.15 ‡
log Clusterin/Cr	-0.072 ‡	0.14*	0.23 *	0.38 ‡
log KIM1/Cr	-0.066 ‡	-0.04	0.074	0.22 †
log Osteoactivin/Cr	-0.015	0.003	-0.015	0.039

log Osteoactivin/Cr	-0.015	0.003	-0.015	0.039
log TFF3/Cr	-0.083 ‡	-0.009	-0.04	0.24 ‡
log VEGF/Cr	-0.056 ‡	0.075	0.059	0.20 ‡
log Calbindin/Cr	-0.015	0.054	0.065	0.026
log _GST/Cr	-0.104 ‡	0.34 *	0.45 *	0.67 ‡
‡ = P<0.001	† = p <0.01	* = P<0.05	Repeat measures ANOVA	

Abstract Number 14

Incidence, Risk Factors and Outcome of Acute Kidney Injury in Very Low Birth Weight Infants

Neha R Patil[1], Rajesh Koralkar[1], Susan Keeling[1], Namasivayam Ambalavanan[1], David J Askenazi[1]

[1]*University of Alabama at Birmingham*

Background:
Premature infants are at high risk of acute kidney injury (AKI). AKI has been shown to be associated with mortality in neonatal and pediatric critically ill populations.

Objective:
To determine incidence, risk factors and outcome of development of AKI in first two weeks of life in very low birth weight (VLBW) infants.

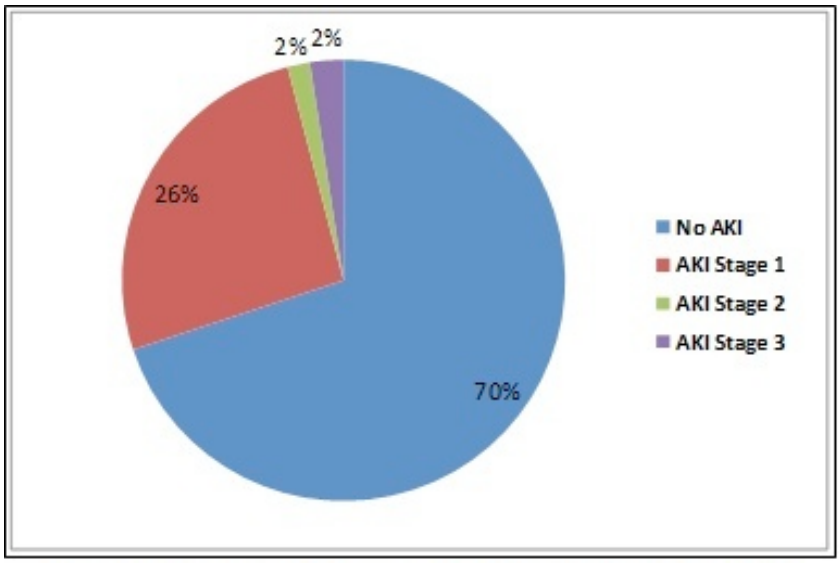
Methods:
• Study Population- 125 Consecutive VLBW Infants (birth weight <=1200 gm. or gestational age <31 weeks) were enrolled between February 2012 and June 2013.
• Definition of AKI- Changes in serum creatinine (SCr) from birth were used to stratify infants into AKI categories according to KDIGO. Stage 1 AKI was defined as SCr > 0.3 mg/dl or > 150-200% from lowest previous value. Stage 2: SCr > 200-300% from previous value and Stage 3 AKI: SCr > 2.5 mg/dl or SCr > 300% from previous value. SCr and urine was obtained on days 1,2,3,4, and 12 on most infants in addition to any clinically measured values.
• We looked at infant and maternal demographics and co-morbidities to determine differences between AKI and No AKI group and their outcomes. Bronchopulmonary dysplasia (BPD) was defined if an infant was oxygen dependent at 36 week post-menstrual age (PMA).

Results:
Cumulative Incidence of AKI in our study was 15% by day 3, 26% by day 7 and increased to 30% by day 15 of life (Figure 1). Lower gestational age, lower birth weight and umbilical artery catheterization (UAC) were risk factors for AKI (p value <0.05). Pre-eclampsia was inversely associated with AKI (p value <0.001). Those with AKI have higher incidence of BPD/Mortality at 36 weeks PMA(53% vs. 30%) and trend towards longer hospital stay compared to those without AKI (Table 1).

Conclusion:
AKI is common in VLBW infants. Cumulative incidence of AKI over first two weeks of life was 30%. Lower birth weight, UAC, and lack of preeclampsia were independent predictors for AKI (p value <0.05). Development of AKI was associated with BPD/mortality independent of confounding variables. AKI was associated with mortality; however, we are not able to show an independent association between AKI and mortality.

figure on following page

Outcome	AKI (N=36)	No AKI (N=86)	p value
BPD / Mortality at 36 weeks PMA	19/36 (53%)	26/86 (30%)	0.01
Survived or Discharged home	28 (78%)	79 (92%)	0.03
Length of stay (days)	90 +/- 71	78 +/- 62	0.3



Cumulative Incidence of AKI by Day 15 of Life

Abstract Number 15

Clinician Failure to Document Acute Kidney Injury in the Intensive Care Unit

Joshua S Botdorf[1], Abbasali Akhoundi[1], Gina M Iacovella[1], Pramod K Guru[1], Andrea B Braun[1], Kianoush B Kashani[1]

[1]*Mayo Clinic*

Purpose of the study: Acute kidney Injury (AKI) is a common syndrome in the Intensive care unit and is associated with high mortality. Small changes in renal function and serum creatinine are clinically significant, and will meet criteria of Acute Kidney Injury by the Acute Kidney Injury Network (AKIN). However, these changes can be overlooked and the presence of AKI can go unnoticed. Diagnoses and early recognition of AKI poses an opportunity for intervention. This retrospective analysis is aimed at evaluating the discordance in the presence of AKI by AKIN criteria and the diagnosis by clinicians. Methods: Patient records from January to March of 2010 were retrospectively evaluated for those admitted to medical and surgical ICUs with a Foley catheter. Exclusion criteria included those with known AKI or endstage renal disease. All included patients were reviewed by two independent investigators who ascertained the presence of AKI using the AKIN criteria; discordant cases were resolved by a nephrology specialist; this is considered the gold standard. The inter-observer agreement between the two independent reviewers was excellent (k= 0.965; 95% confidence interval [CI] = 0.94 - 0.99). Of those with AKI, the electronic medical records, including clinical notes, intake/output charts, and laboratory data were interrogated for first documentation of AKI. Both urine output criteria and creatinine criteria were used. Data was analyzed using chi-square goodness-of-fit test. Summary of the results: 639 patients were reviewed to enroll 483 patients in the final analysis after removing patients with exclusion criteria. Two hundred seventy-one patients (56.1%) were male with a median age of 66 years (Interquartile range (IQR) 49-75), median Acute Physiology and Chronic Health Evaluation III (APACHE III) score of 59 (IQR 47-72), median Sequential Organ Failure Assessment (SOFA) score of 4 (IQR 2-6), and 413 (89%) were Caucasians. One hundred ninety-three (39.9%) patients were deemed to have AKI by the gold standard. Clinical diagnosis of AKI was documented in 143 (29.6%) as compared to 193 (39.9%) true cases ($p<0.0001$). In the medical, surgical, and mixed medical-surgical ICU's the clinician diagnosis of AKI was 29%, 30.9%, and 28.6%, respectively. This is while the reviewer diagnosis of AKI was 37.0%, 44.3%, and 38.1%. Conclusion reached: Clinicians were significantly unsuccessful in documenting the presence of AKI in the Medical and Surgical ICU environments.

Abstract Number 16

Acute Kidney Injury in "Low-Risk" Patients in Intensive Care

Florentina E Sileanu[1], Raghavan Murugan[1], Nicole Lucko[1], John A Kellum[1]

[1]*University of Pittsburgh Center for Critical Care Nephrology, CRISMA*

Purpose: Critical illness is a major predisposing factor for acute kidney injury (AKI). However, AKI may also be the first manifestation of critical illness. We sought to examine the risk of AKI and outcomes associated with AKI in patients with and without cardiovascular or respiratory organ failures.
Methods: We used the 8-year High-Density Intensive Care (HiDenIC-8) database for our analysis. This database includes 45,655 adults admitted to one of eight intensive care units (ICU) in a single large academic medical center. From this database we assembled two cohorts of patients based on the presence or absence of mechanical ventilation, or use of vasopressors. We defined AKI by KDIGO criteria and compared rates, severity and outcomes of AKI across groups. Our primary endpoint was moderate to severe AKI (Stage 2-3). Finally, we constructed multivariate models to explore which factors were associated with any observed differences.
Results: After excluding patients with AKI Stage 2-3 prior to ICU admission, end-stage renal disease, baseline serum creatinine ≥ 4 and those with insufficient data, 40,152 remained, of which 18,016 (45%) received neither mechanical ventilation nor vasopressor support in the first 24 hours after ICU admission. Stage 2-3 AKI occurred within 24hrs or one week in 14.3% and 25.7% of low-risk patients compared to 29.1% and 65% in patients with respiratory or cardiovascular organ failures. Patients developing AKI had increased risk of death by hospital discharge and by 30, 90 and 365 days compared to those not developing AKI. Relative risks for death at these time points associated with AKI were greater for patients without respiratory or cardiovascular organ failures. Relative risks for death prior to hospital discharge in low-risk compared to high-risk patients were 4.3 vs. 2.0; and 3.2 vs. 1.9 at 30 days.
Conclusion: Patients admitted to the ICU without respiratory or cardiovascular organ failure are still at high risk for AKI. Moreover, although survival for low-risk patients with AKI is better than for high-risk patients with AKI the relative risk for mortality associated with AKI is actually greater for low-risk patients compared to those with respiratory or cardiovascular failures.

Abstract Number 17

Risk Factors for Acute Kidney Injury in the Lushan earthquake victims

Li Zhang[1], Yizhi Chen[1], Ying Zhen[1], Nannan Wang[1], Dong Zhang[1], Jingping Pan[2], Xiuming Xi[3], Jizong Zhao[4], Ziwu Zhang[2], Xiangmei Chen[1]

[1]*Chinese PLA General Hospital,* [2]*Sichuan provincial health bureau ,* [3]*Beijing Fuxing Hospital ,* [4]*Beijing Tiantan Hospital*

Purpose
Acute kidney injury (AKI) is a lethal but reversible complication after an earthquake. At 08:02 Beijing Time on 20 April 2013, a 7.0-magnitude earthquake hit Lushan county of Ya'an city in south China's Sichuan province. A total of 196 people had been confirmed dead, 21 missing and 11470 injured. This study aims at identifying risk factors for AKI in the Lushan earthquake victims.
METHODS
We retrospectively analyzed the Lushan earthquake trauma database. The victims with at least two records of serum creatinine within the 7 days were included in the study. AKI was defined according to the current KDIGO consensus definitions. We excluded patients younger than 15 years. The subjects included 32 patients AKI patients and 193 victims without AKI. Clinical and laboratory characteristics of the victims were analyzed. Binary logistic regression was used to obtain an adjustment of the estimated odds ratio and find which risk factors were independently associated with AKI. We used a p-value below 0.05 as significant.
RESULTS
No differences in age (50.5±18.8 vs. 50.1±19.9) and gender (68.8% vs. 61.1% male) were found between patients with and without AKI. Among eight patients presenting with shock at admission, five victims developed AKI. Patients who developed

AKI had more severe trauma (Shock index 0.77 vs. 0.64, P=0.001), more multiple trauma (46.9% vs. 18.7%, P=0.001), more head injury (37.5% vs. 17.6%, P=0.001) and more chest trauma (31.3% vs. 17.1, P=0.05) compared with the victims without AKI. Eleven patients suffered crush injury, only three developed AKI. Among patients with AKI, stage 1 comprised 53.1%, while stage 2 and stage 3 were 34.4% and 12.5%, respectively. In terms of outcomes, none of the patients in the present study required renal replacement therapy. Two patients with AKI died in hospital, whereas no patient without AKI died. Multivariate logistic regression analysis indicated that multiple trauma, non fracture injury and higher shock index are independent risk factors for developing of acute kidney injury in the Lushan earthquake victims
CONCLUSIONS
Multiple trauma, non fracture injury and higher shock index are independent risk factors for developing of acute kidney injury in the Lushan earthquake victims.

Abstract Number 18

Concordance of pRIFLE Criteria for Identification of Acute Kidney Injury in Pediatric Patients Following Cardiopulmonary Bypass Cardiac Surgery

Myriam Bransi[1], Jean-Philippe Proulx-Gauthier[1], Dennis Bailey[1], David Simonyan[2], Marc-André Dugas[1]

[1]Centre Mère Enfant Soleil du CHU de Québec, [2]Centre de Recherche du CHU de Québec

Acute kidney injury (AKI) is a frequent complication following cardiopulmonary bypass (CPB) in pediatric patients. The pediatric Risk Injury Failure Loss End-stage renal disease (pRIFLE) definition based either on a serum creatinine increment (SCr) or on low urine output (UO) threshold, is now used to stratify patients with AKI. However, it is not clear if these two criteria identify the same patients. Therefore, we wish to verify the concordance of the pRIFLE UO and SCr criteria, the latter used as gold standard, to identify patients with AKI.

This retrospective single-center study included patients aged from 0 to 18 years who underwent cardiac surgery with CPB between May 2009 and 2011. Exclusion criteria were death during surgery, preoperative chronic kidney failure and anterior heart transplant. Data abstracted from medical records were independently verified by two observers. Patients were divided into non-AKI and AKI subgroups (AKI-Risk, AKI-Injury, AKI-Failure) using the pRIFLE SCr and UO criteria. The McNemar test was applied to show concordance between groups while Cohen Kappa coefficient was used to measure the inter-rater agreement between definitions. ROC curves were used to identify the most predictive diuresis cut-off values to predict pRIFLE SCr AKI.

Among the 141 patients, 50 (36%) met the AKI group according to pRIFLE SCr Risk definition. In the AKI-Risk category, the sensitivity of the UO definition to predict SCr AKI was 36% and the specificity was 93% (McNemar $p<0.0001$, Kappa = 0.33). The AKI-Injury UO definition had sensitivity of 27% and 98% specificity (McNemar $p = 0.03$, Kappa = 0.32). Finally, the AKI-Failure UO definition had sensitivity of 6% and 100% specificity (McNemar $p<0.001$, Kappa = 0.09). ROC curves revealed that the most predictive diuresis cut-off values to predict pRIFLE SCr AKI-Risk, AKI-Injury and AKI-Failure are 0.3 ml/kg/h for 2h (sensitivity 50%, specificity 80%, AUC 0.70), 0.6 ml/kg/h for 12h (sensitivity 47%, specificity 86%, AUC 0.75) and 0.6 ml/kg/h for 11h (sensitivity 56%, specificity 84%, AUC 0.71), respectively.

As shown in this study population, AKI is highly prevalent and the concordance and inter-rater agreement between UO and SCr criteria is poor. Moreover, the accepted diuresis cut-off of the pRIFLE definition may not be adequate. Hence, UO and SCr are not interchangeable criteria in patient selection for clinical studies. More studies are needed to confirm the best diuresis cut-off values.

Abstract Number 19

Epidemiology of Acute Kidney Injury Following Cardiopulmonary Bypass in Pediatric Cardiac Surgery Patients

Myriam Bransi[1], Jean-Philippe Proulx-Gauthier[1], Dennis Bailey[1], David Simonyan[2], Marc-André Dugas[1]

[1]Centre Mère Enfant Soleil du CHU de Québec, [2]Centre de Recherche du CHU de Québec

Acute kidney injury (AKI) is an important complication following cardiopulmonary bypass in pediatric cardiac surgery patients. However, its prevalence is highly variable in studies depending on the choice of AKI definition. Therefore, we aim to describe the epidemiology and outcome associated with AKI according to the accepted pediatric Risk Injury Failure Loss End-stage renal disease criteria (pRIFLE) in our postoperative population of pediatric cardiac surgery patients.

Patients from 0 to 18 years of age admitted to our PICU after cardiac surgery with cardiopulmonary bypass between May 2009 and May 2011 were included in this retrospective cohort study. Data were abstracted from the medical records and independently validated by two observers. Exclusion criteria were death during surgery, preoperative chronic kidney failure and prior heart transplant. Patients were classified according to the pRIFLE categories of risk, injury and failure before comparing their outcomes. Descriptive analyses were based on one-way analysis of variance F-test with correction for unequality of variances when appropriate.

Of the 141 patients who met the inclusion criteria, 59 met the pRIFLE definition for AKI, representing a prevalence rate of 42%. Compared to the non-AKI group, AKI patients were younger (median 0.5 [IQR 0.01-1.41] vs 1.8 [IQR 0.72-8.07] years, $p<0.0001$), had higher Pediatric Risk of Mortality (PRISM) scores (median 10 [IQR 8-13] vs 8 [IQR 6-10], $p<0.05$), higher maximal serum creatinine levels (mean 56 [95% CI, 48-63] vs 37 [95% CI, 33-40] umol/L, $p<0.0001$), longer intensive care unit length of stay (mean 129 [95 % CI, 95-163] vs 58 [95% CI, 40-75] hours, $p<0.05$), longer mechanical ventilation duration (mean 57 [95% CI, 26-89] vs 21 [95% CI, 5-37] hours, $p<0.05$) and longer duration of cardiopulmonary bypass (mean 142 [95% CI, 125-159] vs 95 [95% CI, 85-106] minutes, $p>0.05$). One patient in each group died.

AKI is highly prevalent following cardiopulmonary bypass in pediatric cardiac surgery. Increasing severity of AKI is associated with longer duration of cardiopulmonary bypass, longer intensive care unit length of stay and duration of mechanical ventilation. Specific modifiable risk factors and therapeutic approaches for AKI still need to be identified in order to prevent and treat AKI in this specific population.

Abstract Number 20

Prognostic Value of Dysnatremia in Patients in Need of Renal Replacement Therapy in intensive care units

elizabeth Maccariello[1], Renata Mendes[1], Carla Valente[2], Eduardo Rocha[3], Márcio Soares[4]

[1]Universidade do Estado do Rio de Janeiro, [2]Rede D' Or de Hospitais – Rio de Janeiro, RJ, Brazil, [3]Hospital Universitário Clementino Franga Filho, [4]Instituto D' Or de Pesquisa

Background and objectives

Dysnatremias are the most common electrolyte disorders and an independent risk factor of poor prognosis in critically ill patients. Hyponatremia is more frequent and associated to greater mortality in long-term hemodialysis patients. The present study aims to evaluate the impact of dysnatremia on the prognosis of acute kidney injury (AKI) patients requiring renal replacement therapy (RRT) in the ICU.

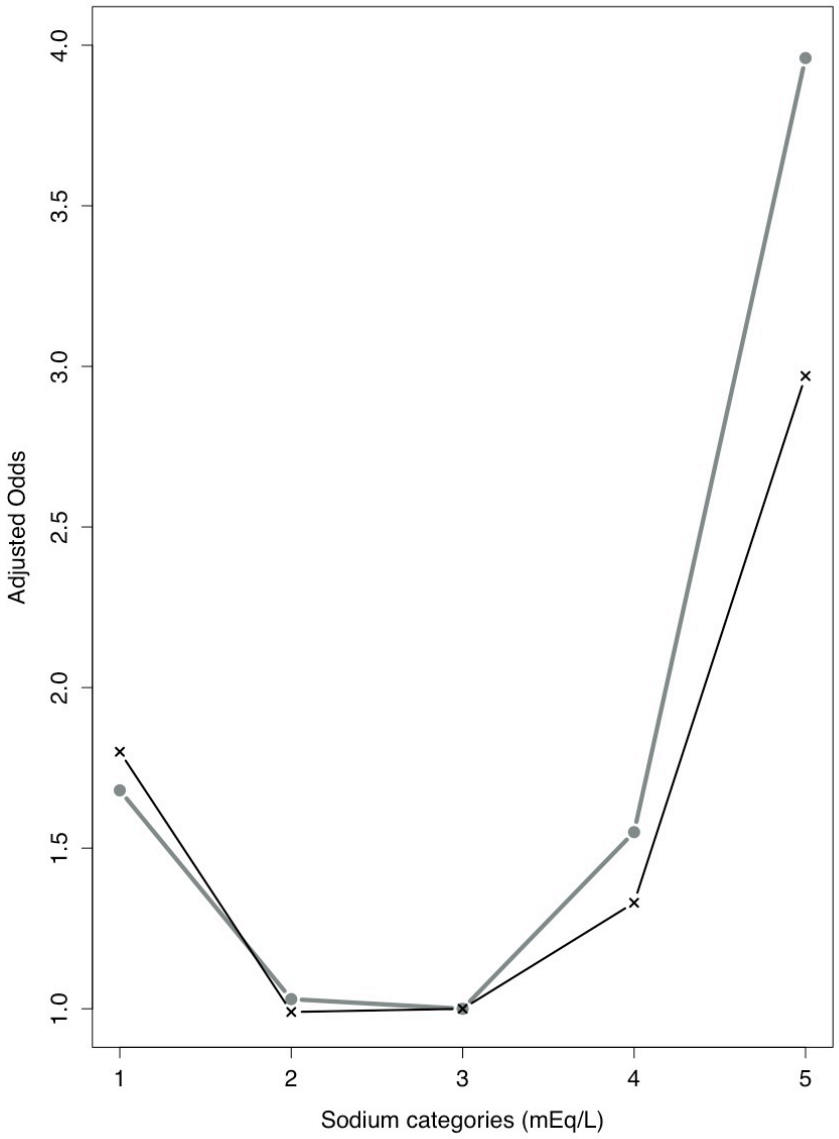
Design, setting, participants, & measurements
A total of 772 patients who were candidates for starting renal RRT and thus made, at three tertiary hospitals of Rio de Janeiro-Brazil, were prospectively included. Sodium measurements were categorized immediately before RRT initiation. Multivariable logistic regression was used to estimate the effect of sodium categories on ICU and hospital mortalities.

Results

Hypernatremia was the main observed sodium disturbance (33.7% hypernatremia X 13,6% hyponatremia), in contrast to published results in the ICU and in chronic hemodialysis patients . In multivariate analysis, dysnatremia, older patients, clinical admission, the number of comorbidities, length of ICU stay before the beginning of RRT and the number of organ dysfunction were associated with higher hospital mortality. Patients with moderate (146-155 mEq/L) and severe (more than 155 mEq/L) hypernatremia showed association with UCI mortality (OR, 1.55; 95% CI, 1.01-2.38 and 3.96; 95% CI, 1.67-9.37 respectively). Severe hypernatremia was also associated with higher mortality (OR, 2.97; 95% CI, 1.22-7.22) Figure 1.

Conclusion

Hypernatremia was the main sodium disturbance and independently associated to poor outcomes in the AKI population in need of RRT in the ICU.



Abstract Number 21

Acute Kidney Injury in the Intensive Care Unit of an Inner City Teaching Hospital

Tanvi Rege[1], Siddhartha Yedla[1], Elizabeth Phipps[1], Oriade Adeoye[1], Shivakanth Burugu[1], Anjali Acharya[1]

[1]*Jacobi Medical Center*

Background: Acute kidney injury (AKI) is associated with bad outcomes, more so in the critically ill patients. The aim of the study was to evaluate outcomes of patients who developed AKI in an inner city intensive care unit (ICU). Patients were identified using electronic medical records in this observational study. Patients were considered eligible if they developed AKI as defined by AKIN criteria, within seven days of ICU admission. Our cohort consists of 847 of the 880 eligible patients admitted to the medical intensive care unit (MICU) at Jacobi Medical Center between April 2009 and October 2013. 173 of 847 critically ill patients (20.4%) had AKI within seven days of ICU admission. Individual records were investigated in detail for demographic as well as medical variables.
Results: Eighty four percent of our patients were non- Caucasian. Sixty three percent had a history of hypertension. Sepsis was seen in 59% of our patients with AKI. Fifty nine percent of the patients had predisposing risk factors for AKI with 82% of them having AKI risk factor exposure in the preceding 4 weeks. SOFA score at AKI start was 5.5 (+/-3.6), Non-renal SOFA score at AKI start was 3.8 (+/-3.3) and Apache III at AKI start was 57.3 (+/-29.1. Mortality rate was 33% in our center.
Conclusion: Ours is a predominantly non Caucasian population with 20.4% of ICU patients developing AKI within seven days of ICU admission. High exposure to AKI risk factors in the preceding 4 weeks played a role in the AKI development. The worse outcomes with non-recovery in our patients could be attributed to accompanying sepsis and hypotension in our baseline hypertensive population. Identifying and appropriately managing the risk factors early in the ICU is crucial for better outcomes.

Characteristics	Jacobi Medical Center
AKI risk factors at screening, %	59
H/o renal insult in preceding 4 weeks, %	82
Sepsis, %	59

Abstract Number 22

Characteristics of Patients with Community-Acquired Acute Kidney Injury

T. Clark Powell, MPH[1], Gaurav Jain, MD[1], David G Warnock, MD[1], Henry E Wang, MD, MS[1]

[1]*University of Alabama at Birmingham, Birmingham, AL, USA*

Introduction: Acute Kidney Injury (AKI) frequently occurs in the inpatient setting and is associated with poor short and long-term outcomes. AKI acquired before hospitalization is increasingly being recognized, but has not been well characterized. We compared inpatient characteristics for persons whose serum creatinine (sCr) improved after admission to an urban academic medical center.

Methods: We analyzed 2011-2012 hospital discharge and serum creatinine data from the University of Alabama at Birmingham Hospital (UAB). We included all adult inpatients with at least two sCr measurements. We excluded patients <18 years of age and patients with a history of end-stage renal disease or kidney transplant. We defined resolving, community acquired AKI as a sCr decrease ≥0.3mg/dl from the first inpatient sCr. We excluded those with inpatient AKI as defined by an absolute increase ≥0.3mg/dl from the lowest of the first three sCr. We defined chronic kidney disease (CKD) as estimated glomerular filtration rate <60mL/min/1.73m2 as calculated from first hospital sCr. We limited analysis to the first 22 days of hospitalization or the first 60 sCr. We analyzed patient characteristics, AKI incidence, and inpatient mortality rates for those with community acquired AKI compared to those with no AKI.

Results: The analysis included 38,042 admission events that met the inclusion criteria. Individuals with AKI present before

hospital admission compared to those without AKI were older (59 vs 56, p<0.0001), had shorter length of hospital stay (2 days vs 3 days, p<0.0001), had higher baseline sCr (2 vs 1.2, p<0.0001), had higher peak sCr (2 mg/dl vs 1.2 mg/dl, p<0.0001), were more likely to be male (54.8% vs 51.1%, p=0.005), were more likely to be of Black race (41.7% vs 33.8%, p<0.0001), were more likely to have chronic kidney disease (72.1% vs 26.9%, p<0.0001), and were less likely to spend time in an Intensive Care Unit (6.7% vs 18.9%, p<0.0001). Inpatient mortality was similar between those with AKI present before admission and those without AKI (1.9% vs 1.6%, p=0.32).

Conclusions: AKI present prior to hospital admission is not associated with increased inpatient mortality, as has been previously reported for those who develop AKI during hospitalization. Patient demographics, ICU admission rates, and baseline kidney function differ between those with community-acquired AKI and those without AKI.

Abstract Number 23

Acute Kidney Injury - A Tale of Two Medical Centers

T Clark Powell, MPH[1], Gaurav Jain, MD[1], David G Warnock, MD[1], Joseph Abdelmalek, MD[2], Ravindra L Mehta, MD[2], Henry E Wang, MD, MS[1]

[1]University of Alabama at Birmingham, Birmingham, AL, USA, [2]University of California, San Diego, San Diego, CA, USA

Introduction: Acute Kidney Injury (AKI) is common and associated with significant short and long-term sequelae. While prior studies have characterized AKI among hospitalized patients, there are few comparisons of AKI between patient populations at different centers. We compared inpatient baseline characteristics and AKI incidence rates between two urban academic medical centers.

Methods: We analyzed 2011-2012 hospital discharge and serum creatinine (sCr) data from two urban academic medical centers: University of Alabama at Birmingham Hospital (UAB) and University of California San Diego Medical Center (UCSD). We included all adult inpatients with at least two sCr measurements. We excluded patients less than 18 years of age and patients with a history of end-stage renal disease or kidney transplant. We defined chronic kidney disease (CKD) as estimated glomerular filtration rate <60 mL/min/1.73m2 as calculated from first hospital sCr. We defined AKI as a sCr increase ≥0.3mg/dl from the lowest of the first three inpatient sCr. We limited analysis to the first 22 days of hospitalization or the first 60 sCr. We compared patient characteristics, AKI incidence and inpatient mortality rates at both centers.

Results: The analysis included 39,920 qualifying admission events from UAB and 15,596 from UCSD. AKI rates differed between centers (UAB 22.4% vs. UCSD 17.9%, p<0.0001), but had similar associated inpatient mortality (UAB 10.3% vs UCSD 9.2%, p=0.08). Compared with UAB, UCSD AKI patients were older (62 vs. 58 years, p<0.0001), more likely to be male (60.1% vs. 51.5%, p<0.0001), had a higher prevalence of CKD (55.5% vs 45.1%, p<0.0001), were less likely to spend time in an ICU (17.8% vs 40.9%, p<0.0001), exhibited higher peak sCr (3.3 mg/dl vs 2.3 mg/dl, p<0.0001), and had longer time to peak sCr (3 days vs 2.6 days (p<0.0001). Length of hospital stay among AKI patients was similar between centers (7 days vs 7 days, p=0.07).

Conclusions: AKI was common at both medical centers, and associated with similar, high rates of inpatient mortality despite differences in demographics and ICU admission rates between centers. These results illustrate the value of multicenter data collection and analysis in characterizing AKI epidemiology and identifying novel risk factors for inpatient AKI.

Abstract Number 24

Incidence o Acute Kidney Injury Following Left Ventricular Device Implantation: Cleveland Clinic Experience

Sevag Demirjian[1], Diana Dietzer[1], Maria M Mountis[1], Brian R Stephany[1]

[1]*Cleveland Clinic*

Purpose of the study
Advanced heart failure is often complicated by the development of renal failure and is associated with high mortality. In recent years, there has been increased use of left ventricular assist device (LVAD) as bridge to transplant or as destination therapy. We studied pertinent renal variables and outcomes pre and post-LVAD surgery.
Methods
We studied all patients who underwent continuous LVAD implantation between the years 2001 and 2013 at Cleveland Clinic. Estimated renal function was calculated using CKD-EPI equation.
Results
Three hundred and thirteen patients underwent LVAD implantation with mean age of 54 ± 14 years; 18% were African-American; 82% were male. Mean pre-operative creatinine was 1.4 ± 0.5 mg/dl. 48% of subjects had pre-operative GFR less than 60 ml/min/1.73m2. In the two weeks following LVAD implantation, 25 patients (8%) doubled their creatinine, and 30 (10%) required renal replacement therapy.
Conclusion
Preoperative renal impairment is common in patients undergoing LVAD implantation and we observed high incidence of post-operative severe acute kidney injury.

Abstract Number 25

Continuous Renal Replacement in Pediatric Patients with Acute and Acute-on-chronic Liver Failure

Keila L De La Garza[1], Alyssa Riley[1], Poyyapakkam Srivaths[1], Carolyn Smith[2], Mary N Watson[2], Amelia Allstead[2], Helen Currier[2], Ayse Akcan Arikan[1]

[1]*Baylor College of Medicine,* [2]*Texas Children's Hospital*

Acute and acute-on-chronic liver failure (LF) can lead to multiple organ failure and associated acute kidney injury (AKI) requiring renal replacement (CRRT) therapy in the pediatric population. AKI in LF is multifactorial with hepatorenal syndrome, nephrotoxic medications, abdominal compartment physiology, and intrinsic renal dysfunction. The natural progression of this disease process is detrimental with high mortality despite maximum support. We retrospectively reviewed patients with LF who received CRRT over the last three years in our institution. Charts of patients who required CRRT for primary or secondary LF-related complications between 2011-2013 were reviewed. There were 45 patients, 31 % were male; mean age was 6.7 ± 7.2 years. 19/45 pts (42%)were less than 2 years old. All pts were mechanically ventilated, mean length of ventilation was 19.2 ± 14.5 days. 64% received at least one vasoactive amine. CRRT was provided as continuous venovenous hemodiafiltration (CVVHDF). Blood-primed circuits were used in all pts < 15 kg. Regional anticoagulation with citrate was used for all stand-alone CRRT. Median length of CVVHDF was 9 days (IQR 5, 20). 28 pts died (62%). Eleven pts received intermittent hemodialysis as well as CRRT, 6 of these were converted to IHD at PICU discharge, three pts liberated from IHD and one patient remained IHD dependent at hospital discharge. The other 2 pts who are IHD dependent are still in-house. All of the pts who required IHD at PICU discharge were less than 2 years old. The mean length of hospital stay was 52.8 ± 44.5 days. The average percent fluid overload (FO%= total fluidin-total fluid out/PICU admission weight) was 21.3 ± 19% at CRRT initiation. Nine pts had a FO %> 25%, 6 of these patients died, the other three remained IHD dependent at PICU discharge. Only 19 pts had complete information available regarding citrate toxicity, seven patients were noted to have “citrate lock” by nephrologists in the charts. Common interventions were decreasing citrate dose, increasing diffusive clearance, and transiently stopping citrate (2 pts). No treatments were interrupted because of citrate toxicity. LF-related AKI requiring CRRT has a very high mortality and morbidity. Younger cohort makes CRRT treatment technically challenging and may necessitate further IHD at PICU discharge. Long term close follow-up of these pts is essential. Regional citrate anticoagulation seems safe in this population although further studies are needed.

Abstract Number 26

RETROSPECTIVE ANALYSIS OF AKI INCIDENCE AND DIALYSIS MODALITY IN PATIENTS WITH MULTIPLE MYELOMA (MM): IMPACT ON OUTCOME AND RESIDUAL RENAL FUNCTION

Alessandro D Quercia[1], Sergio Dellepiane[1], Davide Medica[1], Massimo Gai[1], Vincenzo Cantaluppi[1]

[1]*Nephrology, Dialysis and Kidney Transplantation Unit, University of Torino*

BACKGROUND AND AIM OF THE STUDY
Acute kidney injury (AKI) is a frequent complication of patients with Multiple Myeloma (MM). AKI is consequent to the development of proximal tubular cell apoptosis and cast nephropathy for light chain deposition.
Aim of the study was the monocentric retrospective analysis of AKI incidence and dialysis modality in patients with MM and the evaluation of outcome and impact on residual renal function.
METHODS
We retrospectively evaluated patients with MM-associated AKI in the period 2011-2012 in accordance to RIFLE criteria and presence of Bence-Jones (B-J) proteinuria. Bone marrow biopsy and serum/urine immunoelectrophoresis were performed. In case of dialysis, high cut-off (HCO: Theralite Gambro) or enhanced adsorption (EA: PMMA Toray or PEPA Nikkiso) hemodialyzers were used and serum free light chains (FLC) were evaluated (Freelite).
RESULTS
We enrolled in the study 69 patients with MM characterized by the following parameters at admission: proteinuria 7.8±3.2 g/24h, B-J proteinuria 42%, main types of MM: IgGK 46%, IgA_ 30%. Diagnosis of AKI was reported in 21/69 patients (30.4%). RIFLE criteria (based on serum creatinine) were distributed as follows: 14.3% Risk, 19% Injury, 66.7% Failure. The most used therapeutic approaches in AKI patients were bortezomib, thalidomide and dexamethasone (66.6%) associated with stem cell autografts (90.5%). Six MM patients with AKI (28.6%) required dialysis. HCO hemodyalizers were used in the majority of cases inducing a reduction of serum FLC of about 50-60%. A significant reduction of FLC was also observed using EA filters. Outcome of MM patients with AKI at 1 year from the study admission was: dead 23.8% (5/21), survivors 76.2% (16/21). In survivors, serum creatinine was 2.26± 1.02 mg/dl, eGFR 33±15 ml/min
CONCLUSIONS
AKI is a common complication of patients with MM and it is often associated with worse outcome and with a rapid progression toward chronic kidney disease, in particular when the need of dialysis occurred. Early interventions with hematologic therapies, stem cell autografts and FLC removal by dialysis with HCO/EA membranes may improve MM patients' outcome.

Abstract Number 27

Comparison of Absolute vs Relative Increases in Creatinine to Define Acute Kidney Injury

Joana Balderas Juarez [1], Armando Vazquez Rangel [1]

[1]*Instituto Nacional de Cardiologia Ignacio Chavez*

Introduction. Current KDIGO criteria for defining acute kidney injury (AKI) include the relative elevation of serum creatinine (SCr) and an absolute increase only for the first stage. Waikar et al have proposed that absolute increases can reduce biases due mainly to the baseline renal function.
Objectives. To compare the incidence of AKI and mortality defined by relative (KDIGO) vs absolute (Waikar) increments in SCr; and to assess the added value of their combination.
Methods. An ambispective cohort study in adult patients admitted to the intensive care unit (ICU) after cardiac surgery in a third-level academic center in Mexico City from March 1st 2010 to June 30th 2012. We excluded patients with chronic kidney disease (CKD) stage 5, preoperative AKI, minimum invasive procedures, intraoperative death or during the first 24 hrs. SCr was measured in an every-day basis and adjusted for fluid balance.
Results. We analyzed 794 patients. The incidence of AKI stages 1, 2 and 3 was 20.8, 2.1 and 7.3 percent based on KDIGO, and 11.2, 2.9 and 7.1 percent based on absolute increases. The overall agreement was 87.9 percent, with a Kappa of 0.713. Within KDIGO stage 1, the mortality was 8.5, 6.2 and 15.4 percent if they had no AKI by absolute criteria, stage 1 or severe AKI

(stage 2-3) respectively. The 2x increase in SCr was equivalent in mortality to an increase of 0.5mg/dL in 48hrs. The addition of the latter to KDIGO stage 2 criteria showed an OR of 2.9 (p=0.027) adjusted for age, gender and baseline renal function. ROC curves comparing original and modified KDIGO criteria were not different (AUC 0.713 and 0.714 respectively for death). Finally, the time for detection of severe AKI was in average 0.5 days earlier adding the absolute increase in 0.5 mg/dl in 48 hrs as KDIGO stage 2 (p=0.015), which was more significant in patients with CKD.
Conclusions. AKI defined only by absolute increases in SCr (Waikar) underestimated the incidence. Severe AKI by absolute criteria contributes to a high mortality in spite of being in non-severe stage for KDIGO. The addition of 0.5 mg/dl in 48 hrs for severe AKI reclassified a limited number of patients without improving its performance, however it allows to identify severe AKI in a significantly shorter period of time.

		Cr_KDIGO				
		No AKI	AKI 1	AKI 2	AKI 3	Total
Cr_Absoluto	No AKI	554 (69.8%)	71 (8.9%)	1 (0.1%)	0 (0.0%)	626 (78.8%)
	AKI 1	0 (0.0%)	81 (10.2%)	7 (0.9%)	1 (0.1%)	89 (11.2%)
	AKI 2	0 (0.0%)	13 (1.6%)	8 (1.0%)	2 (0.3%)	23 (2.9%)
	AKI 3	0 (0.0%)	0 (0.0%)	1 (0.1%)	55 (6.9%)	56 (7.1%)
	Total	554 (69.8%)	165 (20.8%)	17 (2.1%)	58 (7.3%)	794 (100.0%)

Abstract Number 28

Mexican Survey on Current Practices in Acute Kidney Injury in Critically Ill Patients: From the AKIMEX Collaborative Group

Armando Vazquez-Rangel[1], Manuel Poblano[2], Maria Elena Reyes[3], Alberto Carrillo[3], Erick Vidal[4]

[1]Instituto Nacional de Cardiologia, [2]Hospital Juarez de Mexico, [3]Centro Medico Nacional La Raza, [4]Hospital Angeles Lomas

PURPOSE: There is not enough information on practices in acute kidney injury (AKI) in developing countries. A survey on this topic represents a starting point to diagnose areas of opportunity and to plan next steps for research.

METHODS: From November 2012 to November 2013 an online survey assessing 32 aspects regarding AKI and Renal Support Therapy (RST) in Intensive Care Units (ICU) was available for departments of Intensive Care Medicine or Nephrology in training centers in Mexico.

RESULTS: A total of 14 centers for Nephrology and 16 for Intensive Care Medicine (87.5 and 47.0% of available training centers in our country) answered the survey. Participants have 200-399 hospital beds, 10-19 ICU beds, 40-59% of surgical patients, 5-9 cases of AKI per month and 3-5 cases requiring RST. Most common baseline conditions were sepsis and cardiovascular disease. In 4 (13.3%) novel biomarkers are used to identify AKI. Most common criteria to start RST were serum creatinine and fluid overload. In general, 26 (86.7%) use RIFLE/AKIN criteria for starting RST. All centers have IHD available, 10 (33.3%) have SLED, 18 (60.0%) have CRRT and 19 (63.3%) have PD, while actual use was reported in 68.6%, 7.1%, 18.0% and 6.3% respectively; if there were no limitations, 73.3% would choose CRRT as their first option. Most common complications were hemodynamic instability for IHD and SLED, filter clotting for CRRT, and inadequate clearance

for PD. The reasons for choosing CRRT were: higher clearance, efficient ultrafiltration, multi-organ protection, renal recovery, less complications, and hemodynamic stability; For choosing IHD were: equipment availability and more experience; For choosing PD were: no need for anticoagulation; As other reasons intensivists considered that PD was cheaper, while nephrologist thought that this was the case for IHD, and intensivists mentioned there is more evidence in favor of CRRT, while nephrologists consider there is more for SLED. Intensivists consider that in 20-39% of AKI cases nephrologists are consulted, while nephrologists think that consultation occurs in 60-79% (p=0.03).

CONCLUSIONS: A high frequency of AKI is expected in future epidemiology studies. There is a trend to support treatment decisions on RIFLE/AKIN criteria. Although CRRT is recognized to have more benefits, current use is limited maybe due to low experience or availability. There is a need for standardization and integration between intensivists and nephrologists.

RESEARCH IN AKI

Abstract Number 29

Survival Advantage for High Dose Bicarbonate in CKD Patients Undergoing Angiography: the BOSS trial

Richard Solomon[1], Harold L Dauerman[1], Paul Gordon[2], Steven V Manoukian[3], J Dawn Abbott[4], Dean J Keriakes[5], Allen Jeremias[6], Michael Kim[7]

[1]University of Vermont College of Medicine, [2]Mirian Hospital, Providence, RI, [3]Tristar Centennial Medical Center, Nashville, TN, [4]Rhode Island Hospital, Providence, RI, [5]Ohio Heart and Vascular Center, Cincinnati, OH, [6]Stony Brook Heart Institute, Stony Brook, NY, [7]Mount Sinai Hospital, NYC, NY

Background: Contrast-induced acute kidney injury (CI-AKI) is associated with adverse effects. The role of bicarbonate prophylaxis for prevention of CI-AKI is controversial and heterogeneity may be due to dose differences. We tested the role of high dose bicarbonate for the prevention of chronic kidney injury, dialysis, and death.
Methods: BOSS was scheduled to enroll 536 high-risk patients (GFR < 45) undergoing angiography randomized 1:1 to high dose bicarbonate (~2.0 mEq/kg) versus an identical dosing regimen of intravenous normal. The study was powered to show a significant difference in the primary endpoint of death, dialysis or 20% reduction in GFR at 6 month follow up, with secondary analysis of 72 hour CI-AKI (> 25% rise of creatinine from baseline).
Results: 391 of 536 (73%) of patients were randomized prior to the scheduled interim analysis. 15 subjects did not have angiography leaving 376 in the ITT analysis. Baseline characteristics and risk factors for endpoints were similar between the two arms. The primary endpoint occurred in 60 total patients (~16%) through 6 months of follow up but was not different between treatment arms. CI-AKI (72 hours) occurred in 39 patients (~11%) in both arms. In subjects that had coronary angiography, a 69% reduction in death at six months for the bicarbonate treated subjects was seen. Mortality was not related to the occurrence of either acute kidney injury or a 20% loss of kidney function at 6 months. The DSMB recommended stopping the trial for futility based upon the primary endpoint.
Conclusions: The incidence of six-month persistent contrast induced kidney injury (consecutive elevations of sCr or dialysis) was roughly 10% among these high-risk patients and the odds ratio was 2.75 in the group with AKI. However, the complication of persistent kidney injury is not prevented to a greater extent with bicarbonate as compared to the identical high dose regimen using saline hydration. The survival advantage associated with bicarbonate infusion was highly significant (p=0.021). It was seen only in the patients (n=299) who underwent coronary angiography. A meta-analysis of bicarbonate-saline trials in this population reporting on mortality confirmed the survival advantage at both 30 days and 1 year with point estimates of 0.5 (95% CI: 0.3-0.85) and 0.45 (95% CI: 0.29-0.76) respectively. Further trials are needed to confirm the survival advantage and better understand potential mechanism of this effect.

Abstract Number 30

EFFICACY OF CONTINUOUS HAEMODIAFILTRATION USING A POLYMETHYLMETHACRYLATE MEMBRANE HAEMOFILTER _PMMA-CHDF_IN THE TREATMENT OF SEPTIC SHOCK AND ACUTE RESPIRATORY DISTRESS SYNDROME(ARDS)

Masahito Sakai[1]

[1]*Shintakeo hospital*

CHDF using with a polymethymethacrylate membrane is currently widely applied for non-renal indications in Japan, this technique is used in the treatment not only of patients with sepsis but also of those with cytokine-induced critical illness such as ARDS and pancreatitis. The main underlying mechanism governing cytokine removal through PMMA-CHDF is the adsorption of cytokines to the hemofilter membrane and this characteristic was not observed in the other membrane material.
This study aimed to investigate the clinical efficacy of PMMA-CHDF in the treatment of a patients with septic shock and ARDS .
Eighty patients diagnosed with septic shock (ARDS[n=45], Pyelonephritis
[n=10], Cholangitisn [n=5], Tsutugamusi in Scrub typhus disease[n=1],Snake Mamushi biten[n=1], haemophagocytic syndrome[n=1],anti neutrophil cytoplasmic antibody(ANCA)lung disiese[n=1],beriberi heart disease[n=1] and unknown causes[n=15])were enrolled in this study between August 2010 and November2013.The common cause for ARDS in elderly patients aspiration pneumonia in elderly patients. Our study group composed 40men and 40women, aged 35 -85 years(median age 68years).
Before initiating treatment with the PMMA-CHDF,the average Acute Physiology and Chronic Evaluation(APACHE)score of these patients was 17.5+/-3.6 ,whereas the average Sepsis-related Organ Failure Assessment(SOFA)score was 6.5+/-1.3. The duration of PMMA-CHDF treatment was5.2+/-2.3days.
Following initiation of PMMA-CHDF teatment, early improvement of haemodynamics was observed,along with an increase in the urine output. The average survival rates of patients were75.6%. The low survival rate among diseases 35% belonged to the Unknown group. The highest survival rate for patients with ARDS was 95%.Moreover,the urine output significantly increased in survival group.
The present study suggests that cytokine-oriented critical care using PMMA-CHDFmight be effective the treatment of sepsis and ARDS,
particularly,in the treatment of ARDS associated with aspiration pneumonia in elderly patients.

Abstract Number 31

Renal Biomarker Levels in a Child Presenting with Newly Diagnosed Acute Lymphoblastic Leukemia and AKI Secondary to Tumor Lysis Syndrome

Richard M Hackbarth[1], Robert K Fitzgerald[1], Akunne N Ndika[1], Chi L Braunreiter[1], Julia M Steinke[1], Dawn M Eding[1]

[1]*Helen DeVos Children's Hospital*

Acute Leukemia is the most common malignancy of childhood. Children presenting with acute leukemia are susceptible to acute kidney injury (AKI) due to multiple factors including, infiltration of the kidneys with leukemic cells, dehydration, tumor lysis syndrome (TLS), and nephrotoxic medications. Creatinine is a relatively insensitive measure of AKI. The expression of newer, novel biomarkers such as NGAL, IL-18, and KIM-1 is markedly induced in the renal tubule during AKI. These biomarkers have not been studied in leukemia associated renal injury.
Methods: We report the time course of three novel urinary biomarkers in a child with newly diagnosed acute lymphoblastic leukemia (ALL) presenting with TLS and AKI by pediatric RIFLE criteria. The child required CRRT for 20 hours following hospital admission, but was off all RRT by the start of chemotherapy. Urine NGAL, IL-18, and KIM-1 were measured pre-chemotherapy and following initiation of IV induction therapy at 6, 12, 24 hours, daily for the first week, and weekly for the next 3 weeks. Biomarkers were analyzed by ELISA and data normalized for urine creatinine.
Results: Urine NGAL peaked at 1170 ug/mg Cr (4-fold rise) 12 hours post chemotherapy and returned to baseline by day 7. KIM-1 peaked at 5083 pg/mg Cr (12-fold rise) on day 5 and returned to baseline by week 4. IL-18 peaked at 180 pg/mg Cr on day 3 (2-fold rise), returning to near baseline by day 7 but increased again at week 2 which was temporally associated with

pseudomonas bacteremia (Table 1). Serum creatinine consistently declined throughout the course of chemotherapy despite these changes in other renal biomarkers. The patient's renal function by RIFLE criteria was RIFLE-I at the start of chemotherapy and returned to normal by day 4 of induction chemotherapy.
Conclusions: In this child with new onset ALL and AKI secondary to TLS, a significant elevation in novel renal biomarkers was noted following initiation of IV chemotherapy despite improving estimated creatinine clearance (eCCL). We postulate that this change represents subtle, secondary tubular injury by nephrotoxic agents in an already vulnerable host. The role of novel renal biomarkers in elucidating renal injury in children with TLS at time of induction chemotherapy deserves further investigation.

Table 1

Biomarker	Pre-Chemotherapy	Post Induction Peak
eCCL by Schwartz	51*	58*
NGAL[1]	309	1170
KIM-1[2]	3098 (406 at 12 hrs induction)	5083
IL-18[2]	86	180

1- microgram/ mg Cr
2- picogram/ mg Cr
*- lowest clearance value post induction in mL/min/m2

Abstract Number 32

Subclinical And Clinical Contrast-Induced Acute Kidney Injury: Results From The ENCINO Study

Krittapoom Akrawinthawong[1], Jason Ricci[2], Louis Cannon[2], Simon Dixon[3], Kenneth Kupfer[4], Gillian Parker[4], David Stivers[4], Patrick Alexander[5], Shukri David[5], Peter McCullough[5]

[1]St.John Hospital & Medical Center, [2]McLaren Northern Michigan Hospital, [3]Oakland University William Beaumont School of Medicine, William Beaumont Hospital, [4]Alere North America, [5]Providence Hospitals and Medical Centers

Background. Neutrophil gelatinase-associated lipocalin (NGAL, siderocalin-2) is produced by distal renal tubular cells in response to injury. Contrast-induced acute kidney injury (CI-AKI) is associated with adverse in-hospital and long-term outcomes in chronic kidney disease (CKD) patients. We sought to characterize blood NGAL level and the degree of kidney injury reflected by further increases in NGAL and conventional definitions of CI-AKI in CKD patients who underwent coronary angiography.

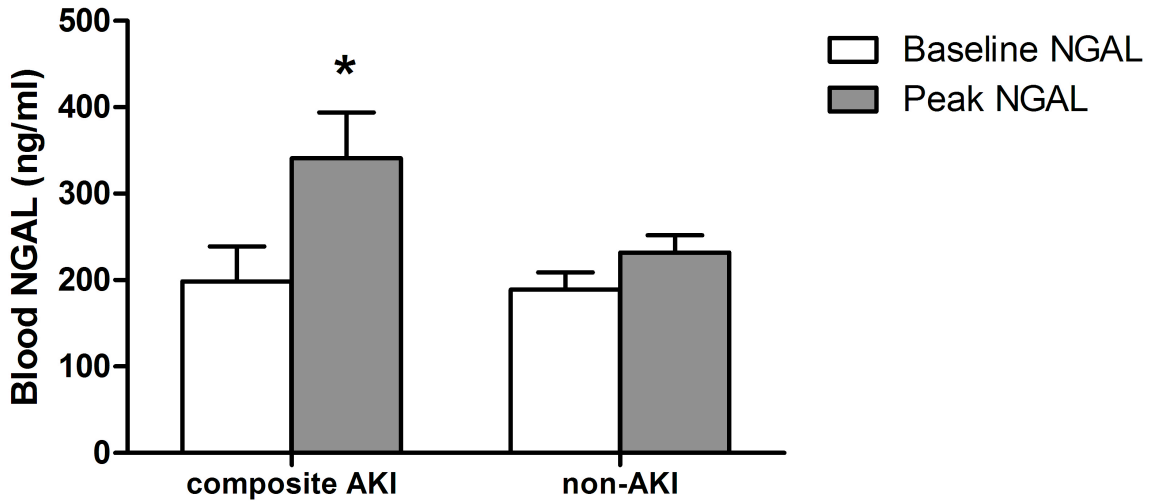
Methods. This study was a prospective, blinded assessment of blood samples obtained from patients with estimated glomerular filtration rates (eGFR) between 15 and 90 ml/min/1.73 m2 undergoing elective coronary angiography with iodinated contrast. Renal transplant recipients, dialysis patients, and those who had received iodinated contrast within 30 days were excluded. Blood NGAL was measured using a commercially available assay and serum creatinine (Cr) was measured using isotope dilution mass spectrometry traceable methods at a core laboratory. Samples were obtained at baseline, 1, 2, 4, 6, 12, 24, and 48 hours after contrast administration.

Results. A total of 63 subjects were enrolled with a mean age of 69.43±9.32 years and a mean eGFR of 48.17±16.45 ml/min/1.73 m2. There was a graded increase in baseline NGAL levels across worsening stages of CKD (p=0.0001). Post-procedure NGAL increased from baseline in each stage of CKD. Eight (12.7%) patients were diagnosed with CI-AKI by diagnostic criteria of 2012 Kidney Disease International Global Outcomes (KDIGO) definition of CI-AKI, and 7 (11.1%) developed subclinical CI-AKI defined by a twofold or greater rise in NGAL. Two subjects met both creatinine and NGAL criteria. Binary logistic regression found no relationship between baseline eGFR or diabetes, two traditional CI-AKI risk predictors, on the composite outcome.

Conclusions. Baseline and post-procedure NGAL are progressively elevated according to the baseline stage of CKD. Using a twofold rise in NGAL, 46.7% of composite CI-AKI is detected and complements the 53.3% of cases identified using KDIGO criteria. When using a composite of subclinical and clinical CI-AKI, traditional risk predictors (eGFR and diabetes) were not

independently associated with this outcome.

Baseline eGFR Range (ml/min/1.73m2)	All (N=63) 15.7-83.8	15-30 (N=9) 15.7-26.9	30-45 (N=21) 30.7-44.0	45-60 (N=18) 49.8-59.2	60-90 (N=15) 62.2-83.8	p-value
Age	69.43 ± 9.32	69.00 ± 11.88	70.62 ± 9.98	68.11 ± 9.50	69.60 ± 6.88	0.873
Male	46 (73.0)	7 (77.8)	15 (71.4)	12 (66.7)	12 (80.0)	0.843
Female	17 (27.0)	2 (22.2)	6 (28.6)	6 (33.3)	3 (20.0)	0.843
White	54 (85.7)	6 (66.7)	19 (90.5)	15 (83.3)	14 (93.3)	0.128
Black	8 (12.7)	2 (22.2)	2 (9.5)	3 (16.7)	1 (6.7)	0.128
Other Race	1 (1.6)	1 (11.1)	0 (0)	0 (0)	0 (0)	-
Diabetes	22 (34.9)	7 (77.8)	5 (23.8)	7(38.9)	3 (20.0)	0.630
Atrial Fibrillation	7 (11.1)	3 (33.3)	4 (19.0)	0 (0)	0 (0)	-
Weight (kg)	155.21±65.93	185.33 ± 45.87	134.24 ± 61.95	134.83 ± 72.71	190.93 ± 54.80	0.014*
SBP (mmHg)	146.27±29.83	150.56 ± 31.84	158.38 ± 35.36	138.11 ± 17.20	136.53 ± 28.22	0.083
DBP (mmHg)	80.05±13.57	79.22 ± 18.70	82.00 ± 12.00	76.67 ± 12.99	81.87 ± 13.42	0.613
Cr (mg/dl)	1.54±0.49	2.40 ± 0.30	1.73 ± 0.28	1.30 ± 0.18	1.04 ± 0.17	0.0005*
BUN (mg/dl)	27.66±12.37	39.67 ± 15.68	31.97 ± 12.51	24.11 ± 7.07	18.67 ± 5.46	0.0003*
eGFR CKD EPI	48.17±16.45	26.36 ± 4.38	37.17 ± 4.81	53.07 ± 5.03	70.76 ± 7.68	0.0005*
Base NGAL(ng/ml)	191.32±141.92	360.29 ± 227.94	224.72 ± 117.43	132.29 ± 67.88	114.02 ± 57.42	0.0001*
Iso-osmolar contrast	28 (44.4)	9 (100.0)	10 (47.6)	5 (27.8)	4 (26.7)	0.001*
contrast volume (ml)	131.87±66.19	80.22 ± 39.69	126.71 ± 62.39	134.61 ± 65.07	166.80 ± 68.75	0.017*
1455.31 ± 826.19	1088.88 ± 714.61	770.86 ± 777.47	973.00 ± 543.41	1074.56±770.76	Pre-procedure iv fluid (ml)	0.0004*
3 (20.0)	5 (27.8)	14 (66.7)	8 (88.9)	30 (47.6)	Prophylactic NAC	0.137



Abstract Number 33

Actual Versus Ideal Body Weight For Acute Kidney Injury Diagnosis In Critically Ill Patients

Wisit Cheungpasitporn[1], Charat Thongprayoon[1], Abbasali Akhoundi[1], Kianoush B Kashani[1]

[1]*Mayo Clinic, Rochester, MN*

Background: According to urine output (UO) definition in KDIGO criteria to diagnose and stage acute kidney injury (AKI), it is unclear which body weights (BW), actual versus ideal body weight, should be used to diagnose and stage AKI, leading to heterogeneity cross research studies.

Method: This is a single-center retrospective observational study conducted at a tertiary referral hospital. All adult patients who were admitted to intensive care units (ICU) at our institution for a minimum of 6 continuous hours between January and February 2010 were eligible for this study. Only patients who had urinary catheter were included. Patients who had an end stage renal disease or needed a dialysis before ICU admission were excluded. AKI stages based on UO definition was assessed by calculating UO per kilogram per hour, with actual versus ideal body weight.

Result: A total of 493 ICU patients were included in analysis. The median actual and ideal BW were 82 (IQR 68-96) and 70 (IQR 60-77) kg respectively. Using ideal BW, AKI could be diagnosed in 154(31.2%) patients and 204(41.4%) using actual BW (p-value < 0.01). Patients who had AKI regardless of BW calculation methodology had relative risk for 90-day mortality of 1.68 (95%CI 1.12-2.54), whereas patients who had AKI according to actual BW but not ideal BW had a non-significant decreased relative risk of 90-day mortality (0.74; 95%CI 0.31-1.79) compared to patients who had no AKI.

Conclusion: Using actual body weight to diagnose AKI by urine output does not add any advantage over the ideal body weight and indeed it may decrease its specificity by adding false positive cases. For this reason we would recommend using ideal body weight to calculate the oliguria for diagnosis of AKI based on UO definition.

Actual body weight	Ideal body weight	N	RR(95% CI)
AKI	AKI	154	1.68 (1.12-2.54)
AKI	No AKI	50	0.74 (0.31-1.79)
No AKI	AKI	0	N/A
No AKI	No AKI	289	Reference group

Abstract Number 34

Change in Intra-Renal Oxygenation by BOLD MRI as Early Marker of Iodinated Contrast Induced AKI (CIAKI)

Lu-Ping Li[1], Jing Lu[1], Tammy Franklin[1], Jon Thacker[1], Maria Papadopulou[1], Richard Solomon[2], Ying Zhou[1], Pottumarthi V Prasad[1]

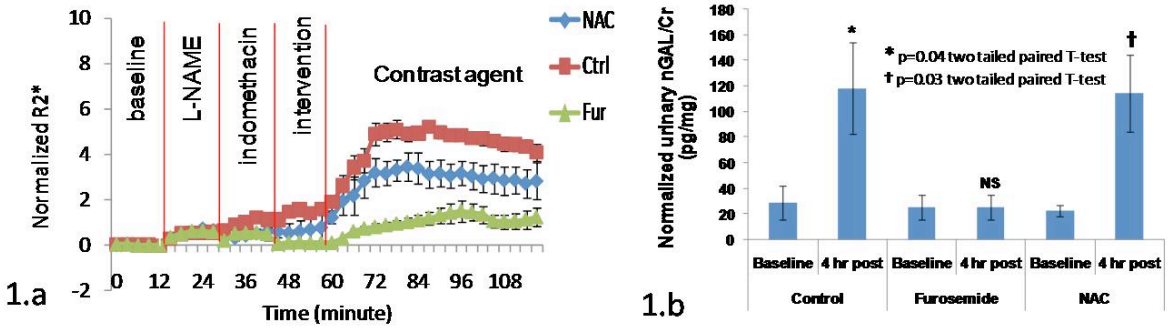
[1]*NorthShore University HealthSystem, Evanston, IL,* [2]*University of Vermont, Burlington, VT*

Purpose: Recent reports have questioned the causality of CI-AKI. This is related to the clinical definition of CIAKI based on delayed serum creatinine measurements 48-72 hours post-contrast media (CM). Novel markers such as neutrophil gelatinase-associated lipocalin (NGAL) can detect evidence of injury within hours post-contrast. Previous reports using blood oxygenation level dependent (BOLD) MRI have shown near real-time responses to iodinated contrast in CIAKI susceptible rats. The purpose of this study was to evaluate whether the BOLD MRI response observed post-CM in CIAKI susceptible animals leads to AKI as determined by urinary NGAL and if this can be reversed by targeted interventions.

Methods and Materials: Male Sprague-Dawley rats (n=18) were anesthetized using inactin (100 mg/kg i.p.) and divided into 3 groups: Control: receiving nitric oxide synthase inhibitor, N-nitro-L-arginine methyl ester (L-NAME, 10mg/kg) and prostaglandin inhibitor, indomethacin (10 mg/kg) followed by saline (1ml/kg) prior to iodixanol (1600 mgI), FUR group: receiving furosemide (10mg/ kg) instead of saline; NAC group: receiving n-acetylcysteine (60mg/kg) instead of saline. Group assignments were made in a random order and blinded fashion. Urine samples obtained at baseline and 4 hours post-CM were used to measure NGAL levels as a marker for renal injury. To account for the variable dilution of urine, NGAL concentrations were normalized to uCr measurements.

Results: Figure shows the changes in R2* (indicating relative level of hypoxia) in the inner stripe of outer medulla (ISOM), found to be the area most sensitive to changes observed in response to pre-treatment and contrast agents. Furosemide did minimize the increase in R2* post-CM compared to control or NAC groups (Figure 1.a). The NGAL elevation was prevented in the FUR group indicating protection from injury (Figure 1.b). NAC (at the dose used) was not effective in providing protection from injury.

Conclusions: For the first time, the observations with BOLD MRI in the model of CIAKI have been compared with an independent biomarker for CIAKI, urinary NGAL. The combined observations show that increased R2* post-contrast do lead to AKI, and support the hypothesis that interventions such as furosemide can improve the oxygenation in ISOM and mitigate CIAKI. Since NGAL has been shown to detect CIAKI in humans, these observations can be translated to humans.



Abstract Number 36

Cell Cycle Arrest Biomarkers Predict Acute Kidney Injury and Survival in Septic Rats

Zhiyong Peng[1], Jicheng Zhang[1], Feihu Zhou[1], John A Kellum[1]

[1]*Center of Critical Care Nephrology,University of Pittsburgh Medical Center*

Purpose: Cell cycle arrest biomarkers, urine insulin-like growth factor-binding protein 7 (IGFBP7) and urine tissue inhibitor of metalloproteinases-2 (TIMP-2), have been recently found to predict acute kidney injury (AKI) in humans. Should they also be validated in animals, these models can be used to explore timing and treatment. In this study we validate these markers in sepsis-associated AKI in rats.

Methods: Sepsis was induced by cecal ligation and puncture (CLP) in adult SD rats. Eighteen hours after CLP, animals were returned to the lab, and fluid resuscitated; then observed for AKI and survival. Blood and urine samples were collected at baseline, 18 hr after CLP, 4 hr after fluid resuscitation, and 24 hr after resuscitation. AKI severity was assessed by RIFLE criteria (creatinine only), which classified risk (R), injury (I), and failure (F), on the basis of maximum creatinine increase of 150%, 200%, and 300%, respectively, in the 2 days following CLP. Urine TIMP2 and IGFBP7 at 4 hr of resuscitation were used to evaluate risk for severe AKI (I+F) and mortality.

Results: About 80% of the rats developed AKI after CLP sepsis. Increased urine TIMP2 and IGFBP7 levels were observed in animals developing severe AKI compared to those that did not (1.61 vs 0.90 µg/ml in TIMP2, and 0.027 vs 0.022 µg/ml in

IGFBP7, P<0.05). The values of urine TIMP2_IGFBP7 were much higher in severe AKI group (0.040 vs 0.019 μg2/ml2, p<0.0001). The receiver-operator characteristic curve (ROC) analysis of urine TIMP2, IGFBP7 and TIMP2_IGFBP7 for severe AKI and non-severe AKI showed areas of 0.76, 0.72 and 0.89 respectively (all p<0.05) . There were significantly higher urine IGFBP7 and TIMP2_IGFBP7 in non-survival animals compared to survival animals (0.028 vs 0.021 μg/ml, and 0.039 vs 0.027 μg2/ml2, p<0.05). The areas under the ROC curves for urine IGFBP7 and TIMP2_IGFBP7 for predicting non-survival were 0.76 and 0.70 (P<0.05).

Conclusion: Urine cell cycle arrest biomarkers, TIMP2 and IGFBP7, are valid biomarkers to detect severe AKI in CLP-induced sepsis. The products of TIMP2 and IGFBP7 are better than individual biomarkers for predicting AKI. This model system can be used for study of sepsis-associated AKI.

Abstract Number 37

AMP-protein kinase activation may protect against sepsis-induced acute kidney injury (AKI) through mechanisms other than energy regulation

Hernando Gomez[1], Daniel Escobar[1], Brian S Zuckerbraun[1]

[1]*University of Pittsburgh*

Background: Sepsis is often associated with organ injury, and particularly with AKI. However, the mechanism of sepsis-induced AKI is incompletely understood. Cellular energy dis-regulation has been suggested to play a role in sepsis-induced organ injury and thus we hypothesized that exogenous activation of AMPK, a master regulator of energy balance, can protect against sepsis-induced AKI.
Methods: Two cohorts of 30 C57BL/6 male mice, 6-8 weeks of age, weighing 20-25g were allocated to six groups. 1. Cecal ligation and puncture (CLP); 2. CLP+AICAR (100mg/kg 24h before CLP; AMPK stimulant); 3. CLP+Compound C (30mg/kg; CoC; AMPK inhibitor); 4. Sham; 5. Sham+AICAR; 6. Sham+CoC. Tissue and blood were collected at 8 hours post-CLP. Renal function was measured with Creatinine (Cr, mg/dL), BUN (mg/dL) and Cystatin C (CysC,ng/mL), cytokine expression with ELISA/ Luminex assay, endothelial activation (ICAM-1 expression), neutrophil adhesion (fluorescence from anti-CD11b mAb-tagged PMNs) and vascular leak (Evan's blue). We reproduced the experiment in vitro using cell culture model (renal epithelial, endothelial cells and macrophages), with similar groups: 1. Control; 2. Control+AICAR (1mM/1h before LPS); 3. LPS (100ng/mL for 4 hours); 4. LPS+AICAR; 5. Control+CoC (10μM/1hr before LPS); 6. LPS+CoC. Cytokines were measured with ELISA. Data presented as mean±SD and as control, LPS/CLP and LPS/CLP+AICAR. *p CLPvs.Control, #CLPvs.CLP+AICAR.
Results: Cr, BUN and CysC were higher in CLP, but not in CLP+AICAR when compared to controls (Cr: 0.16±0.08, 0.43±0.18, 0.2±0.02, p=0.005*, p=0.0003#); BUN: 18±8.0, 62.2±10.8, 43.7±17.7, p<0.001*, p=0.01#; CysC: 29.18±14.5, 103.9±54.8, 49.3±30.8, p=0.007*, p=0.01#, respectively). AICAR also decreased cytokine release in vivo (IL-6, TNFa and IL-10) and in macrophage culture with exception of IL-10 (IL-6: 241.7±1.5 vs 7.2±1.5, p=0.1; TNF: 1882±583 vs 82±28, p=0.04; IL-10: 65.4±1.2 vs 183). AICAR decreased endothelial expression of ICAM-1 in vivo and in vitro, decreased vascular leak (CLP 0.09±0.01 vs. CLP+AICAR 0.06±0.008, p=0.003) and neutrophil adhesion (No. of adhered PMNs: 1055±179 vs. 751±242, p=0.04) in vitro.
Conclusions: AICAR induced AMPK activation, protected against renal dysfunction in the setting of sepsis. AICAR also decreased cytokine release, endothelial activation and vascular leak, suggesting that organ protection may be mediated by modulation of the inflammatory response and protection of the microvasculature.

Abstract Number 38

Genetic Polymorphisms of Heme-oxygenase 1 (HO-1) may Impact on Acute Kidney Injury (AKI), Bronchopulmonary Dysplasia (BPD) and Mortality in Very Low Birth Weight (VLBW) Infants

David J Askenazi[1], Brian Halloran[1], Neha R Patil[1], Rajesh Koralkar[1], Namasivayam Ambalavanan[1]

[1]*University of Alabama at Birmingham*

Background:
HO1 is an enzyme ubiquitously induced in mammalian tissues which catalyzes the rate-limiting step in heme degradation, producing equimolar quantities of biliverdin, iron and carbon monoxide. These products have important anti-inflammatory and anti-oxidant properties which protect against AKI in several animal models. Genetic polymorphisms of HO-1 have been shown to be associated with poor clinical outcomes in several critically ill populations.

Methods:
Population: Between February 2012 and June 2013, VLBW Infants (birth weight ≤1200 gm. or gestational age ≤31 weeks) were prospectively followed.
AKI was defined according to a neonatal AKI definition modified for neonates whereby AKI was defined if serum creatinine (SCr)≥ 0.3 mg/dl or ≥ 150-200% from lowest previous value. SCr values were prospectively collected on days 1, 2, 3, 4, and 14; and combined with clinically measured SCr.
BPD was defined if an infant was receiving oxygen at 36 weeks post menstrual age (PMA).
Evaluation of genetic polymorphisms: DNA was collected using saliva collection kits (Genotek Oragene) and isolated (Qiagen Gentra Puregene). The promoter region GT(n) was determined by capillary electropheresis (Qiagen Type-It Mutation Detect PCR Kit) Figure 1. The number of GT(n) repeats were counted for each infants' alleles and classified as short (≤ 27) or long (> 27). The –413 snp allele (A v T) was documented for each allele using LTI TaqMan Assay. Plasma HO-1 RNA evaluation from day of life 14 was performed by quantitative PCR using TaqMan Primer Probe sets for HO-1 and HO-2 against GAPDH.

Results:
AKI was documented in 36/122 (30%) of the cohort; 15/122 (13%) died, and 36/107 (34%) survivors had BPD. The average numbers of GT repeats were not different by AKI or BPD category. Categories of allele length (SS vs. SL vs. LL) did not differ by AKI, BPD or survival categories. A vs. T at – 413 alleles trended towards a difference for AKI ($p<0.05$), mortality ($p=0.09$), and for the composite of BPD, AKI or mortality ($p=0.07$)(Table 1).

Conclusion:
We did not find an association between the GT(n) tandem repeat of HO-1 and AKI nor BPD. However, we found a trend towards mortality in those with higher mean GT(n) and LL phenotypes. Infants with TT at the -413 SNP had lower incidence of AKI and trend towards lower mortality and composite outcome. We did not find differences in plasma HO-1 RNA and these 2 genetic polymorphisms, nor clinical outcomes studies.

	AA	AT	TT	p-value
AKI Status				0.04
Yes (N= 34)	10 (29%)	20 (59%)	4 (12%)	
No (N= 83)	21 (25%)	34 (41%)	28 (30%)	
BPD status				0.3
Yes (N= 46)	13 (28%)	25 (54%)	8 (17%)	
No (N= 60)	14 (24%)	28 (47%)	18 (30%)	
Mortality				0.09
Yes (N= 12)	5 (44%)	2 (17%)	5 (44%)	
No (N= 105)	26 (25%)	52 (50%)	27 (26%)	
AKI±BPD±Mortality				0.07
Yes (N= 67)	19 (28%)	35 (52%)	13 (19%)	
No (N= 50)	12 (24%)	19 (38%)	19 (38%)	

Abstract Number 39

Comparison of Sustained Hemodiafiltration (SHDF) with Continuous Venovenous Hemodiafiltration (CVVHDF) for the Treatment of Critically Ill Patients with Acute Kidney Injury

Masanori Abe[1], Tatsuhide Azuma[1], Hiroko Suzuki[1], Osamu Oikawa[1], Noriaki Maruyama[1], Kazuyoshi Okada[1], Masayoshi Soma[1]

[1]Nihon University School of Medicine, Tokyo, Japan

Purpose: Despite improvements in medical care, the mortality of the critically ill patients with acute kidney injury (AKI) who require renal replacement therapy (RRT) remains high. We conducted a prospective, randomized study to compare conventional continuous venovenous hemodiafiltration (CVVHDF) with sustained hemodiafiltration (SHDF) in patients who suffered from AKI and were admitted to intensive care unit (ICU).
Methods: In our study, 60 critically ill patients with AKI who required RRT were treated with either continuous venovenous hemodiafiltration (CVVHDF) or SHDF. The former was performed by administering a postfilter replacement fluid at an effluent rate of 25 mL/kg/h, and the latter was performed by administering a postfilter replacement fluid at a dialysate-flow rate of 300–500 mL/min. All the patients underwent SHDF in the ICU for 6–8 h during the daytime on a daily basis.
Results: The baseline characteristics of the patients in the 2 treatment groups were similar. The primary study outcome—survival until discharge from the ICU or survival for 30 d, whichever was earlier—did not significantly differ between the 2 groups: 70% after CVVHDF and 87% after SHDF. The hospital-survival rate after CVVHDF was 63% and that after SHDF was 73% (NS). The number of patients who showed renal recovery at the time of discharge from the ICU did not significantly differ between the two groups. The duration of the ICU stay significantly differed between the 2 treatments (19.3 ± 17.1 days and 13.9 ± 3.9 days, CVVHDF and SHDF, respectively; $p < 0.05$). Although there was no significant difference between the mean number of treatments performed per patient, the mean duration of daily treatment in the SHDF group was 6.5 ± 1.0 h, which was significantly shorter. Although the total convective volumes—the sum of the replacement-fluid and fluid-removal volumes—did not differ significantly, the dialysate-flow rate was higher in the SHDF group.
Conclusions: Our results suggest that SHDF may be a treatment modality that should achieve similar benefits as CRRT in critically ill patients with AKI. However, our study was performed on a small number of patients and was a single-center study; therefore, a randomized, prospective trial comparing the efficacies of SHDF with conventional CRRT in a large cohort of patients is necessary to determine the relative impact of SHDF on renal recovery and mortality.

Abstract Number 40

Urinary TIMP-2 and IGFBP7 as early biomarkers of acute kidney injury and renal recovery following cardiac surgery

Alexander Zarbock[1], Melanie Meersch[1], Christoph Schmidt[1], Sven Martens[1], Jan Rossaint[1], Kai Singbartl[2], Dennis Görlich[1], John Kellum[3], Hugo Van Aken[1]

[1]University of Münster, Münster, Germany, [2]Penn State College of Medicine Hershey, Hershey, PA, USA, [3]University of Pittsburgh, Pittsburgh, PA, USA

Purpose of the study: Difficulties in prediction and early identification of acute kidney injury (AKI) have hindered the ability to develop preventive and therapeutic measures for this syndrome. We tested the hypothesis that a urine test measuring insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2), both inducers of G1 cell cycle arrest, a key mechanism implicated in AKI, could predict AKI in cardiac surgery patients.
Methods: We studied 50 patients at high risk for AKI undergoing cardiac surgery with cardiopulmonary bypass. Serial urine samples were analyzed for [TIMP-2]*[IGFBP7] concentrations. The primary outcome measure was AKI as defined by international consensus criteria following surgery. Furthermore, we investigated whether urine [TIMP-2]*[IGFBP7] could predict renal recovery from AKI prior to hospital discharge.
Results: 26 patients (52%) developed AKI. Diagnosis based on oliguria and/or serum creatinine did not occur until 1-3 days after cardiopulmonary bypass. In contrast, urine concentration of [TIMP-2]*[IGFBP7] rose from a mean of 0.49 (0.24) at baseline to 1.51 (0.57) 4 h after cardiopulmonary bypass in patients who developed AKI. The maximum urinary [TIMP-2]*[IGFBP7] concentration achieved in the first 24 hours following surgery (composite time point) demonstrated an area under

the receiver-operating characteristic curve of 0.84. Sensitivity was 0.92, and specificity was 0.81 for a cutoff value of 0.50. The decline in urinary [TIMP-2]*[IGFBP7] values was the strongest predictor for renal recovery.
Conclusions: Urinary [TIMP-2]*[IGFBP7] serves as a sensitive and specific biomarker to predict AKI early after cardiac surgery and to predict renal recovery.

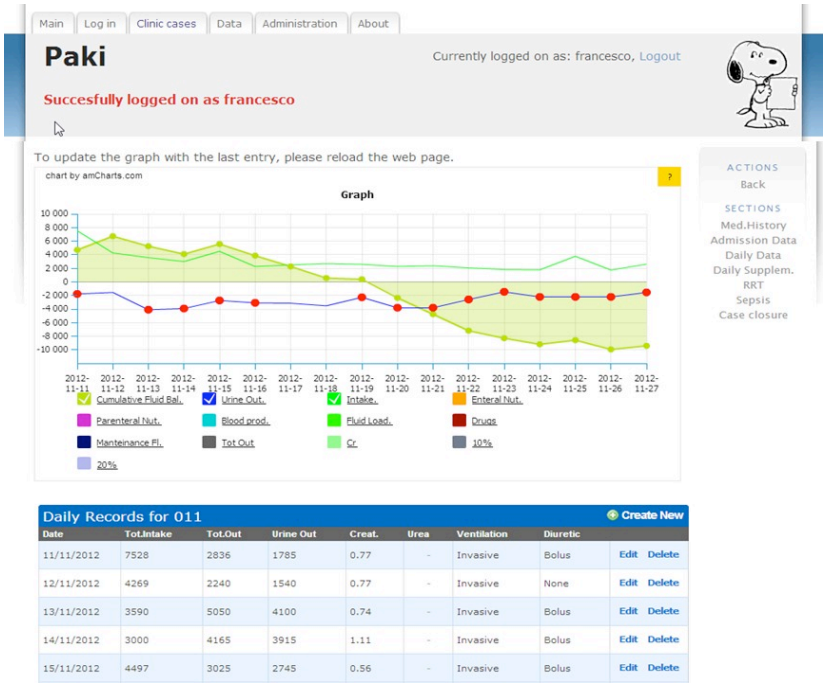
Abstract Number 41

The PAKI (Pediatric Acute Kidney Injury) Registry

Francesco Garzotto[1], Enrico Vidal[2], Monica Zanella[1], Luisa Murer[2], Claudio Ronco[1]

[1]Nephrology, St. Bortolo Hospital, Vicenza, Italy, [2]Pediatrics, University of Padova, Padova, Italy

Background: Advancements and improvements in care for critically ill pediatric population has led to fast changes in pediatric acute kidney injury AKI epidemiology. Prevalent causes leading to pediatric AKI are actually from single center's data. There is also a lack of information concerning AKI patients who did not require CRRT
Objective: The aim of the study is to: describe pediatric AKI patients, identify risk factor for AKI progression, evaluate the influence of fluid overload and type of fluids administrated (colloids, vs crystalloids vs nutrition) on clinical outcomes in AKI (w and w/o RRT) patients, describe current practices of RRT.
Design/Methods: We developed a web-based password protected registry, dedicated to pediatric patients to support an observational and prospective international multicenter study in pediatric intensive care units pICU. Inclusion criteria: all patients admitted to pICU for almost 48h. We daily collect the amount of fluids (intake and output), diuretics, drugs, vasopressors and inotropes as well as scores and type of ventilation. Sepsis has also a dedicated section. RRT page includes dose calculation, circuit type and life, anticoagulants, type and location of catheter. Treatments done with the new carpediem machine also find their location in this section.
Results: After usability test, the registry has been designed on an open source based framework. Automated data verification system, pRIFLE calculation and alert, fluid management graph result as valid supports for fast data analysis helping in daily clinical activities.
Conclusions: The PAKI registry could represent a step forward in the description of the AKI epidemiology in pediatric patients and contribute to the resolution of the controversies regarding CRRT like initiation, dose, technique, anticoagulation.



Date	Tot.Intake	Tot.Out	Urine Out	Creat.	Urea	Ventilation	Diuretic	
11/11/2012	7528	2836	1785	0.77	-	Invasive	Bolus	Edit Delete
12/11/2012	4269	2240	1540	0.77	-	Invasive	None	Edit Delete
13/11/2012	3590	5050	4100	0.74	-	Invasive	Bolus	Edit Delete
14/11/2012	3000	4165	3915	1.11	-	Invasive	Bolus	Edit Delete
15/11/2012	4497	3025	2745	0.56	-	Invasive	Bolus	Edit Delete

Abstract Number 42

Kidney Injury Molecule-1 (KIM-1) Is the Best Urinary Biomarker to Detect Cardiorenal Syndrome In Children with Systolic Left Ventricular Dysfunction

Ahmad Kaddourah[1], Stuart L Goldstein[1], John L Jefferies[2]

[1]Center for Acute Care Nephrology, Cincinnati Children's Hospital Medical Center (CCHMC), Cincinnati, OH, [2]The Heart Institute at CCHMC, Cincinnati, OH.

Introduction and Objectives: Type II cardio-renal syndrome (CRS) describes kidney dysfunction in the presence of chronic heart dysfunction. The role of the novel urinary biomarkers (NUB) has not been investigated in children with systolic left ventricular dysfunction (SLVD). We aim to a) Assess for a correlation between four different NUB and the severity of SLVD, and b) determine if NUB can detect SLVD.
Methodology: We conducted a cross-sectional study in 81 asymptomatic children (aged 1.7 to 21.9 years) with current or previous history of dilated or non-compacted left ventricular etiology. Urine samples were collected to assess the following NUB: KIM-1, IL-18, NGAL and L-FABP. Children had an echocardiogram to measure the left ventricular ejection fraction (EF) on the same day of urine collection. NUB concentrations were adjusted for each mg of urinary creatinine. Univariate regression models were applied to evaluate the correlation between NUB and EF. Univariate analysis was conducted between patients with EF< 55% and EF ≥ 55%. ROC analysis was performed for all NUB to detect EF < 55%.
Results: Forty seven patients (58%) had EF < 55%. The correlation between EF and the four NUB was statistically significant for KIM-1(Table 1). Both KIM-1 and IL-18 concentrations were significantly higher is children with EF<55% vs. EF ≥55% (Table 2). The area under the curve (AUC) of KIM-1 to predict EF < 55% was the best (0.74) compared to IL-18 (0.68), L-FABP (0.56) and NGAL (0.51). The AUC of using both KIM-1 and B-type natriuretic peptide to predict EF < 55% was 0.86.
Conclusion: Our data suggest KIM-1 may be able to detect lower EF in asymptomatic children with dilated cardiomyopathy or left ventricular non-compaction. We suggest elevated KIM-1 in children with EF < 55% patients may signify previously unrecognized CRS and kidney damage.

Table 1: The Correlation between left ventricular ejection fraction (EF) and four novel urinary biomarkers (NUB)			
NUB	_1	R2	P
KIM-1	-0.01	0.13	0.001
IL-18	-0.03	0.04	0.06
NGAL	-0.02	0.01	0.49
L-FABP	-0.25	0.02	0.18

Table 2: The difference in the novel urinary biomarkers (NUB) concentrations between children with left ventricular ejection fraction (EF) < 55% and children with EF ≥55%.			
NUB: median (IQR)	Children with EF < 55%	Children with EF≥ 55%	P
KIM-1 (pg/mg urinary creatinine)	412.9 (248.2 – 606.6)	250.4 (171.3 – 374.6)	0.002
IL-18 (pg/mg urinary creatinine)	48.5 (24.3 – 110.6)	28.2 (17.3 – 37.5)	0.004
NGAL (pg/mg urinary creatinine)	12.9 (6.0 – 48.4)	16.0 (7.3 – 28.3)	0.86
L-FABP (pg/mg urinary creatinine)	3.6 (1.9 – 14.1)	3.3 (1.18 – 8.1)	0.76

Abstract Number 43

Urinary L-FABP Predicts Poor Outcomes in Critically Ill Patients With Early AKI

Sharidan K Parr[1], Amanda J Clark[1], Lorraine B Ware[1], Aihua Bian[1], Ayumi Shintani[1], Nancy E Wickersham[1], T. Alp Ikizler[1], Edward D Siew[1]

[1]*Vanderbilt University Medical Center*

Purpose
Lack of effective treatment for AKI has prompted investigation of novel biomarkers to provide timely diagnostic and prognostic information. Biomarker use for early detection of AKI has shown modest performance, potentially due to uncertainties in using small changes in serum creatinine as a reference and a non-selective approach to testing. Therefore, we hypothesized that targeted measurement in a high-risk population and examination of clinically meaningful endpoints would demonstrate improved utility of these markers. We examined the ability of urine L-type fatty acid binding protein (uL-FABP), neutrophil gelatinase-associated lipocalin (uNGAL), Interleukin-18 (uIL-18), and Kidney Injury Moledule-1 (uKIM-1) to provide prognostic information in patients with early stage AKI.
Methods
The study was performed in the Validation of biomarkers for Acute Lung Injury Diagnosis (VALID) cohort. Adult patients admitted to ICUs at Vanderbilt University were required to have an outpatient baseline creatinine 7-365 days prior to admission and KDIGO Stage 1 injury at the time of biomarker measurement. Biomarkers were examined for independent and combined ability to predict a composite outcome of progression of injury, dialysis, or death in critically ill adults.
Results
A total of 152 patients were included. Thirty-six patients experienced the composite outcome. uL-FABP performed well with an independent area under the receiver-operating characteristic curve (AUC) of 0.79 (95% CI: 0.70-0.86), and improved to 0.82 (95% CI: 0.75-0.90) when added to the clinical prediction model [0.74 (95% CI: 0.68-0.84)], which included age, sepsis, creatinine at biomarker measurement, and APACHE II score. Urine NGAL, uIL-18, and uKIM-1 had AUCs of 0.65 (95% CI: 0.54-0.74), 0.64 (95% CI: 0.53-0.75), and 0.62 (95% CI: 0.53-0.72), respectively, and did not significantly improve the clinical model. Using Integrated Discrimination Index (IDI) and Category Free Net Reclassification Index (cfNRI), uL-FABP had a total IDI of 0.089 (95%CI: 0.034-0.146) and total cfNRI of 42.1%, with a net total of 11.1%(n=4/36) events correctly reclassified to higher risk and 31%(n=36/116) of non-events to lower risk.
Conclusion
uL-FABP independently predicted injury progression or death in critically ill adults with early AKI. Use of early changes in serum creatinine to target measurement of injury biomarkers may enhance the ability of biomarkers to provide timely, meaningful prognostic information.

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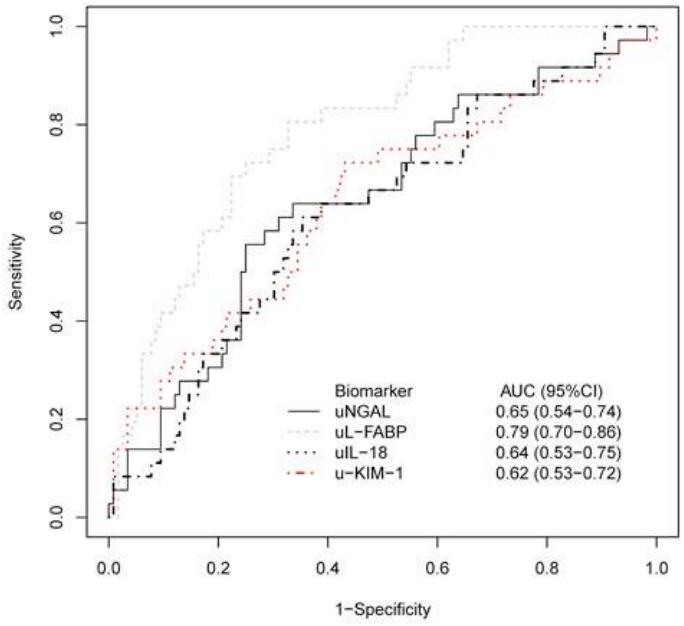
Variable	Composite Outcome (N=36)	No Composite Outcome (N=116)	p-Value
Age	58 (51-67)	61 (53-66)	0.83
Gender			0.43
Female	15 (42%)	40 (34%)	
Male	21 (58%)	76 (66%)	
Ethnicity (%Non-White)	3 (8.3%)	18 (15.5%)	0.28
APACHE II Score	32 (28-37)	27 (21-31)	<0.001
Baseline Sepsis	25 (69%)	55 (47%)	0.021
Creatinine at Study Enrollment (mg/dL)	1.13 (0.90-1.48)	1.19 (0.93-1.50)	0.37
Estimated GFR at Study Enrollment	62 (44-79)	64 (46-82)	0.96
Creatinine at KDIGO Stage 1 AKI (mg/dL)	1.80 (1.47-2.32)	1.73 (1.38-2.19)	0.66
Peak Serum Creatinine (7 days)	2.56 (1.81-3.21)	1.70 (1.32-2.31)	<0.001
uNGAL (ng/mg)	445 (127-1706)	181 (34-421)	0.008
uL-FABP (ng/mg)	459 (192-1558)	107 (42-237)	<0.001
uIL-18 (pg/mg)	458 (281-1232)	294 (156-566)	0.01

uIL-18 (pg/mg)	458 (281-1232)	294 (156-566)	0.01
uKIM-1 (ng/mg)	8.1 (4.2-12.8)	5.4 (2.8-10.2)	0.028
Urine creatinine (mg/ml)	0.68 (0.47-0.84)	0.76 (0.51-1.05)	0.071



Abstract Number 44

Cell-cycle arrest as a mechanism for sepsis-associated acute kidney injury

Xiaoyan Wen[1], Xiaojian Wan[2], Zhiyong Peng[1], John A Kellum[1]

[1]Department of Critical Care Medicine, Center for Critical Care Nephrology, CRISMA, University of Pittsburgh, Pittsburgh, PA, [2]Department of Anesthesiology & Critical Care Medicine, Changhai Hospital, Second Military Medical University, Shanghai, China

Objectives: Markers of G1 cell cycle arrest: Insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2) in the urine have been recently found to predict human AKI. G1 cell cycle arrest has also been implicated as a mechanism of sepsis-associated organ failure. We sought to explore whether this mechanism might play a role in sepsis-associated acute kidney injury (SA-AKI) in an established animal model.
Study design: We randomized 10 male Balb/c mice to receive cecal ligation and puncture (CLP) or sham surgery. Animals were sacrificed 48 hours after surgery and blood was obtained and kidneys removed for histology. Cell cycle arrest was assessed by percent G0-G1. We also performed immunostaining of kidney tissue for IGFBP7 and TIMP2.
Results: Septic (CLP) mice had worse kidney histology score (2.8 vs. 1.4 out of 5) and increase of plasma creatinine (1.2 vs. 0.3 mg/dl) compared to sham. A higher percentage of G0-G1 Cell (95.4% vs. 90.9%) and increased IGFBP7 and TIMP2 staining were found in septic animals compared to sham. The percent of G0-G1 cell in kidney and kidney histology score as well as plasma creatinine concentrations were positively correlated (R2 0.04 and 0.05 respectively).
Conclusion: G1 Cell cycle arrest is a plausible mechanism leading to AS-AKI.

Abstract Number 45

Effects of T-Cell Immune Modulator AB103 on Experimental Sepsis-induced Acute Kidney Injury

Xiaojian Wan[1], Xiaoyan Wen[1], Zhiyong Peng[1], Anat Shirvan[2], Raymond Kaempfer[3], John A Kellum[1]

[1]Department of Critical Care Medicine, Center for Critical Care Nephrology, CRISMA, University of Pittsburgh, Pittsburgh, PA, [2]Atox Bio Ltd, Ness Ziona, Israel, [3]Department of Biochemistry and Molecular Biology, Institute of Medical Research Israel-Canada, The Hebrew University-Hadassah Medical School, Jerusalem, Israel

Objectives: Sepsis is a systemic inflammatory response syndrome caused by severe infection. Sepsis-associated acute kidney injury (SA-AKI) is common and is associated with high morbidity and mortality. However, underlying mechanisms are not completely understood. In response to pathogen-derived molecules, T cell activation plays a crucial role in the immediate immune response. CD28 provides co-stimulatory signals that are required for T cell activation. AB103 is a CD28 dimer interface mimetic peptide that modulates CD28 signaling. We sought to understand the role of AB103 in SA-AKI.
Study Design: Sepsis was induced by cecal ligation and puncture (CLP) in 22 male Balb/c mice of which 6 received sham surgery. Six h after CLP, mice were randomized to receive either a single dose of intravenous AB103 (5 mg/kg) or vehicle, and survival was followed for 48 h. Kidney tissue and blood were collected from surviving animals at that time. Creatinine level and kidney histology were determined, assessing vacuolization of the tubular epithelium/perivascular cell and neutrophil gelatinase-associated lipocalin (NGAL) expression.
Results: Mice subjected to CLP developed severe sepsis roughly 18 h later. Compared to vehicle-treated mice, AB103 treatment significantly increased the survival rate at 48 h (87.5% vs. 42.9%, $p<0.05$). Vehicle-treated septic animals exhibited a significant increase in serum creatinine compared to sham ($P<0.05$) and greatly increased AKI severity, assessed by RIFLE score. By contrast, AB103-treated animals showed no such increases in serum creatinine. However, kidney histology and NGAL expression did not differ significantly between vehicle and treatment groups.
Conclusions: AB103 dramatically improved survival from CLP-sepsis in mice, coupled with significant reduction in serum creatinine.

Abstract Number 46

Urinary NGAL is Elevated in Hospitalized Cystic Fibrosis Patients with Recent and Increased Tobramycin Exposure

Kevin J Downes[1], Marepalli B Rao[2], Michael Bennett[1], Alexander A Vinks[1], Stuart L Goldstein[1]

[1]Cincinnati Children's Hospital Medical Center, [2]University of Cincinnati

Purpose: Patients with cystic fibrosis (CF) are exposed repeatedly to nephrotoxic antibiotics, particularly aminoglycosides. Urinary biomarkers (UB) are sensitive for detecting acute kidney injury (AKI) but values in CF patients have not been previously described. We sought to identify factors associated with UB values during once daily tobramycin (tobra) therapy in CF patients.

Methods: Observational study in CF patients receiving once daily tobra for bronchopneumonia from Oct 2012-Aug 2013. Neutrophil gelatinase-associated lipocalin (NGAL) was measured daily and normalized for urine creatinine (UCr). We examined the association of NGAL concentrations and covariates by applying mixed-effects regression using restricted maximum likelihood (REML) estimation. Secondary analysis, restricted to days on which tobra was measured (N=106), constructed nonparametric ROC curves to determine the optimal NGAL cutoff which identifies increased tobra exposure (AUC>125 mg*h/L). PK parameter estimates were determined using population model-based Bayesian estimation.

Results: 26 patients (median age 15.0 yr, range 3.5-20.8 yr) received 35 tobra courses. Median tobra was 12 days (range 4-22). 5 subjects had AKI (>50% rise in SCr from baseline) within 48 hours of admission, 4 others developed AKI on/after day 3 of tobra (median AKI duration =1 day). Median NGAL for the study population was 53.2 ng/mg UCr (IQR 28.5-101.2) over all study days. Factors associated with higher NGAL levels were female gender (p=.02), increased tobra AUC (p<.01), and recent tobra exposure (p=.03). Low albumin (p=.03) and delta F508 mutation (p=.02) were associated with lower NGAL. The optimal NGAL cutoff to identify AUC>125 mg*h/L by Youden's index was 64.5 ng/mg (sensitivity 84.2%, specificity 64.4%).

Conclusions: We identified several patient- and management-related factors associated with NGAL concentrations during tobra therapy in patients with CF. An NGAL above 64.5 ng/mg may detect supra-therapeutic exposure to tobra as defined by an AUC above 125 mg*h/L. Additional research is needed to determine the role of urinary biomarkers in this high-risk population.

NGAL (ng/mg UCr)	Sens	Spec	LR+	LR-	J-statistic
10.7	1	.06	1.06	0	.06
25.6	.95	.18	1.16	.29	.13
42.6	.89	.49	1.77	.21	.39
64.5	.84	.64	2.36	.25	.49
84.1	.74	.72	2.67	.36	.46
149.6	.47	.90	4.58	.59	.37
256.1	.26	.99	22.90	.75	.25

Abstract Number 47

Performance of Urine TIMP-2 in An Adult Mixed Intensive Care Unit

Tetsushi Yamashita[1], Kent Doi[1], Maki Tsukamoto[1], Masaomi Nangaku[1], Eisei Noiri[1]

[1]*University of Tokyo*

[Background]
Tissue inhibitor of metalloproteinases-2 (TIMP-2), which inhibits not only metalloproteinases but endothelial cell proliferation by binding the integrin alpha3 beta1, was recently reported as a novel biomarker for predicting severe AKI in critical ill patients. We evaluated the performance of urine TIMP-2 in our adult mixed intensive care unit (ICU) by comparing with other biomarkers.
[Methods]
This study enrolled 98 patients who were admitted to the adult mixed ICU of The University of Tokyo Hospital from July 2011 to October 2011 by consecutive sampling. Urine TIMP-2, plasma neutrophil gelatinase-associated lipocain (NGAL) and plasma interleukin-6 (IL-6) were measured on ICU admission. We evaluated whether these biomarkers could predict AKI and its severity, and mortality by receiver operating characteristic (ROC) analysis.
[Results]
AKI occurred in 42 (42.9%) patients including 27 (27.6%) severe AKI (KDIGO stage 2 or 3). The area under the ROC curve for each marker in detecting severe AKI was as follows; urinary TIMP-2 0.80 (0.66–0.90), plasma NGAL 0.87 (0.76–0.93), plasma IL-6 0.69 (0.56 – 0.80). Forty one (41.8%) patients was complicated with sepsis, including 19 (19.4%) severe AKI. In accordance with previous reports, plasma NGAL and IL-6 were increased by sepsis, however urinary TIMP-2 was increased not by sepsis but the presence of severe AKI (Table).
In-hospital mortality was 15.3% in this cohort and urinary TIMP-2 and plasma NGAL were significantly higher in the non-survivors than the survivors, whereas plasma IL-6 was not significantly associated with mortality.
[Conclusion]
A new urine biomarker of TIMP-2 is increased especially in severe AKI and associated with mortality. Sepsis appeared to have a smaller impact on urinary TIMP-2 compared with plasma NGAL and IL-6.

	Sepsis(_) severe AKI(_) (n=49)	Sepsis(+) severe AKI(_) (n=22)	Sepsis(_) sever
Urine TIMP-2 (ng/ml)	1.87 (0.38 – 4.67)	3.43 (1.67 – 5.26)	10.85 (0.71 – 5
Plasma NGAL (ng/ml)	68.00 (60.00 – 129.00)	227.5 (79.50 – 309.75)	211.00 (95.75 -
Plasma IL-6 (pg/ml)	40.04 (18.85 – 195.50)	299.85 (49.73 – 1725.92)	35.85 (20.88 –

Abstract Number 48

Recombinant Alkaline Phosphatase Modulates Inflammation and Injury in Two Rat Models of AKI.

Bulent Ergin[1], Asli Kandil[2], Ebru Gurel[2], Andrea van Elsas[3], Can Ince[1]

[1]Dept. of Translational Physiology, Amsterdam Medical Center, Netherlands, [2]Dept Biology, University of Istanbul. Turkey, [3]AM-Pharma BV, Bunnik, Netherlands

Purified Bovine intestinal Alkaline Phosphatase (BiAP) demonstrated intriguing clinical activity as a potential therapeutic option for sepsis-associated acute kidney injury (Heemskerk et al. 2009, Crit.Care Med. 37: 417; Pickkers et al., 2012, Crit.Care 23:R14). A novel human chimeric recombinant alkaline phosphatase (recAP) was constructed by swapping the stability (crown) domain from human intestinal AP with that derived from human placental AP. Compared to BiAP, recAP retains all enzyme activity but gains in stability and PK properties. To study its therapeutic efficacy and mode-of-action in models of acute kidney injury (AKI), a single i.v. dose of 1000 U/kg recAP was administered to instrumented Wistar rats (7 per group) within 30 min. after induction of AKI by ischemia-reperfusion (I-R) or LPS and compared to saline (n=7). Systemic and local hemodynamics as well as kidney oxygenation were assessed for the duration of the experiment (3 h post-treatment). A control group underwent surgery and insertion of various probes without AKI induction. Saline treated animals developed signs of mild (I-R model) or severe AKI (LPS model). Systemic hemodynamics were unaffected by recAP, however renal vascular resistance improved in the I-R model (control 2424 ± 370 dyn/s/cm2, 4314 ± 1182 in the saline group vs 2905 ± 1246 after recAP treatment) and renal blood flow significantly improved in the LPS model (control 5.02 ± 1.30 mL/min, saline 8.35 ± 2.98, recAP 6.28 ± 1.89, $p<0.01$). RecAP modulated inflammatory markers including iNOS, IL-6 ($p<0.001$), as well as peroxidation marker MDA ($p<0.001$) in the LPS model as demonstrated by immunohistochemistry. Compared to saline, recAP treatment reduced the number of infiltrating MPO+ leukocytes in peritubular areas ($p<0.05$). Moreover, recAP significantly reduced expression of renal injury markers L-FABP, NGAL ($p<0.001$) and pro-apoptic Bax ($p<0.01$). In conclusion, recAP demonstrated immediate pharmacological effect in rat AKI which included suppression of acute inflammation in the afflicted kidney and inhibition of tissue injury. This study provides evidence that recAP is an active protein therapeutic in two rat models of AKI and a first assessment of its mode-of-action.

Abstract Number 49

Transgenic Mice With High Endogenous Omega-3 Fatty Acid Are Protected From Ischemia- Reperfusion-induced Acute Kidney Injury

Won Min Hwang[1], Jaeku Kang[2], Dong Mee Lim[3], Sungro Yun[1]

[1]Department of Nephrology, College of Medicine, Konyang University , [2]Department of Pharmcology, College of Medicine, Konyang University , [3]Department of Endocrinology, College of Medicine, Konyang University

Background: Acute kidney injury (AKI) is common clinical event and has high mortality rate despite advanced curative strategies. Several studies found that omega-3 polyunsaturated fatty acid(PUFA) diet reduces kidney dysfunction followed by ischemic injury. However oral appliance of omega-3 PUFA, in fact, can cause much variability arisen from diet procedure. fat-1 transgenic mouse produce abundant omega-3 PUFA, result in balanced omega-6 : omega-3 ratio than wild type mouse. The purpose of this study, therefore, is to see whether omega-3 PUFA has advantages in AKI caused by ischemic injury using fat-1 transgenic mice.
Methods/Materials: Bilateral kidneys were subjected to 30 min of ischemia, renal ischemia-reperfusion injury(IRI)was performed. Animals(fat-1 mice and C57BL/6 mice) are sacrificed 24hours and 72 hours of reperfusion. The effects of omega-3 PUFA on renal IRI were evaluated in terms of renal function, tubular necrosis, inflammatory cell infiltration. After that,renal function and severity of renal injury were estimated.
Result: fat-1 mice could reduce to increased BUN, serum creatinine and tissue Kim-1 levels(Fig.), and reduce neutrophil infiltration in body after IRI, compared with Wild Type mice.
Conclusions :Long-term and high dose of omega-3 supplement can protect renal function and facilitate renal recovery following IRI.

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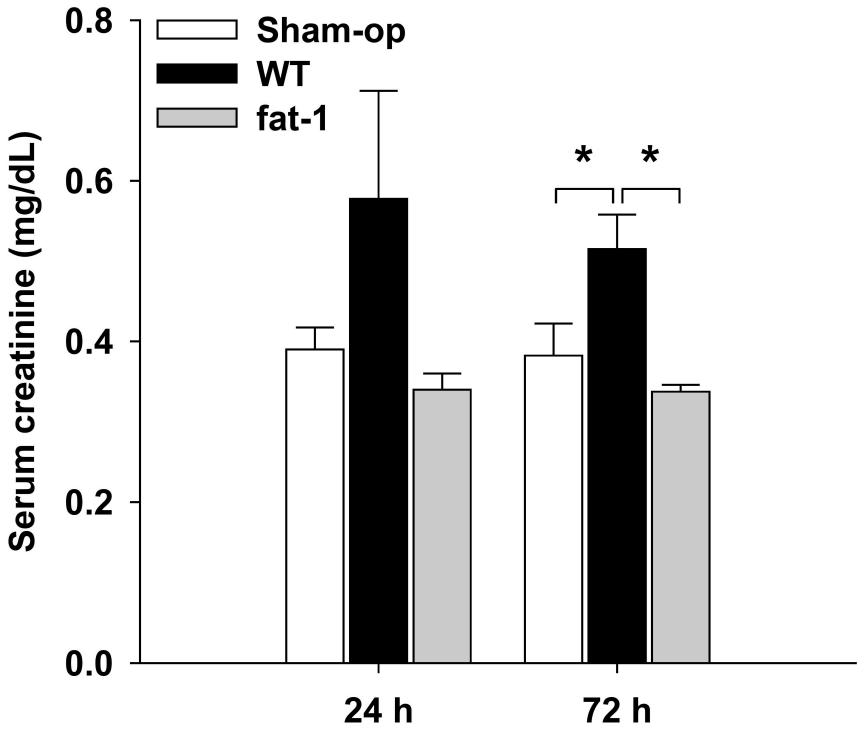


Abstract Number 51

Hyperchloremia and Mortality Outcomes in Critically ill Septic Patients

Javier A Neyra[1], Fabrizio Canepa-Escaro[2], John Manllo[2], Xilong Li[1], Jerry Yee[2], Lenar Yessayan[2]

[1]University of Texas Southwestern Medical Center, [2]Henry Ford Hospital

Sepsis and septic shock are the most common causes of intensive care unit (ICU) admission and are associated with high morbidity and mortality. Hyperchloremia has been recently linked to increased mortality in critically ill patients. This is particularly important considering the common use of chloride-rich solutions in the early phase of resuscitation in sepsis. The aim of this study is to determine if worsening hyperchloremia within the first 72 h of ICU admission is associated with increased in-hospital mortality.

A single center hospital-based linked administrative database of patients with severe sepsis or septic shock admitted to the ICU between July 2007 and April 2012 was retrospectively analyzed. Severe sepsis or septic shock was defined by Angus criteria. Our study group comprised 1,110 patients with available serum chloride on the day of ICU admission (Cl1) and at least one additional value of serum chloride within the next 48 to 72 h of ICU admission (Cl2). The primary independent variable for the analysis was "delta Cl ≥5", defined as the difference between the Cl2 and Cl1. The primary outcome was in-hospital mortality. Mean age (SD) was 65 (15) years: 40% were African American and 36% Caucasian. The mean Cl1 (SD) was 106.5 (7.6) mEq/L and Cl2 (SD) was 107.50 (6.9) mEq/L. Of the 1,110 patients included in the study, 360 (32%) patients had hyperchloremia at the time of ICU admission ("hyperchloremia group" or Cl1 ≥110 mEq/L). When delta Cl ≥5 (Cl2-Cl1) occurred, 95/343 (27.7%) patients died in comparison to 159/767 (20.7%) when it did not [OR 1.46 (1.09-1.96), p =0.01]. The association of delta Cl ≥5 with in-hospital mortality persisted after adjusting for confounders (age, sex, SOFA score, acute kidney injury, cumulative fluid balance at 72 h, and baseline estimated glomerular filtration rate): OR 1.36 (1.00-1.84), p =0.05; more significantly in the "hyperchloremia group" [OR 2.90 (1.37-6.13), p <0.01].

This study highlights the potential association between worsening hyperchloremia (delta Cl ≥5) and in-hospital mortality in critically ill septic patients, particularly in those patients who already have hyperchloremia (Cl1 ≥110 mEq/L) at the time of ICU admission. Further studies are needed to fully elucidate and confirm these findings.

Abstract Number 52

Quorum Sensing (QS) Molecules Released by Gram Negative Bacteria induce tubular injury interacting with lipopolysaccharide (LPS): a new potential mechanism of sepsis-associated AKI

Vincenzo Cantaluppi[1], Davide Medica[1], Viviana T Orlandi[2], Alessandro D Quercia[1], Sergio Dellepiane[1], Giovanni Camussi[1]

[1]Nephrology, Dialysis and Kidney Transplantation Unit, University of Torino, [2]Department of Theoric and Applied Sciences, University of Insubria, Varese, Italy

Background and aim of the study
Quorum sensing (QS) are small diffusible signal molecules adopted by Gram negative and positive bacteria for intercellular communication. Recent studies suggested that QS can interact with eukaryotic cells exerting immunomodulatory effects and playing a key role in urinary tract infection and biofilm formation. QS are also known to bind the lipid A fraction of lipopolysaccharide (LPS).
The aim of this study was to evaluate the potential role of QS in sepsis-associated AKI studying their biological effects on human kidney tubular epithelial cells (TEC).
Methods
Human TEC were isolated from kidneys of patients subjected to nephrectomy. QS from P. aeruginosa were purchased by Sigma Aldrich. In selected experiments supernatants of QS-negative mutants or wild type P. aeruginosa were used on TEC evaluating: cytotoxicity (XTT), apoptosis (TUNEL, caspase-3, -8, 9 activities), cell polarity (trans-epithelial electrical resistance, TEER), ROS production, NGAL mRNA/protein expression, in vitro leukocyte adhesion and FACS/immunofluorescence analysis of molecules typical of fully differentiated TEC (ZO-1, megalin, AQP-2, E-cadherin) or involved in inflammation (ICAM-1, CD40).
Results
QS exerted a dose-dependent cytotoxic and pro-apoptotic effect on TEC inducing Fas and caspase activation. In addition, QS induced in TEC the loss of cell polarity with a decrease of TEER and of expression of ZO-1, megalin and AQP-2 and the concomitant increase of NGAL expression and ROS production. In addition, QS induced a pro-inflammatory effect on TEC increasing leukocyte adhesion and the surface expression of ICAM-1 and CD40. These deleterious effects of QS were enhanced by co-incubation with lipopolysaccharide. Similar effects on TEC were observed using supernatants from QS-negative mutants but not from wild type P. aeruginosa. In addition, QS-induced TEC injury was significantly decreased after pre-treatment of plasma in vitro with polymyxin-B(PMX-B).
Conclusions
Gram negative-derived QS exert a pro-apoptotic and pro-inflammatory effect on TEC in synergy with lipopolysaccharide. Our results suggest a putative role of QS in sepsis-associated AKI. Preliminary analysis by HPLC-MS showed the presence of QS in patients with Gram negative bacteriemia. Last, the binding of QS to lipid A of lipopolysaccharide and the effect observed in vitro may suggest a potential protective role of PMX-B hemoperfusion on QS-induced TEC injury.

RRT TECHNIQUE CHARACTERISTICS

Abstract Number 53

Determining Filtration Fraction for Continuous Veno-Venous Hemofiltration with Replacement Fluid Prefilter Dilution

Carl P Walther[1], Amber S Podoll[1], Kevin W Finkel[1]

[1]The University of Texas Health Science Center at Houston

Background
Filter clotting is a common problem for continuous renal replacement (CRRT) therapies, and the risk of clotting increases with higher filtration fraction (FF). FF should not exceed 20 to 30% to prevent filter clotting. FF is easily calculated for continuous veno-venous hemodialysis, or continuous veno-venous hemofiltration (CVVHF) using post-filter replacement fluid (RF).

However, prefilter RF is sometimes used in CVVHF to decrease FF and thus reduce filter clotting. However, this makes calculation of the FF more complex, and formulae for calculating FF in this setting have not been published to our knowledge.

Methods

FF is the ratio of the rate of fluid removal across a filter to the fluid flow entering the filter. In RRT techniques without significant predilution rates, this is calculated as shown in Eq. 1 , where Quf is ultrafiltration rate and Qp is plasma flow rate. Plasma flow rate is calculated as shown in Eq. 2, where Hct is hematocrit and Qb is blood flow rate. In CVVHF, Quf is equal to the sum of the net ultrafiltration rate (Qufnet) and the replacement fluid rate (Qrf) (see Eq.3). In CVVHF with predilution replacement fluid, where (as in most machines) the clinician sets the "blood flow rate," which actually sets the rate of flow of the mixture of blood and predilution fluid, effective plasma flow rate is calculated as shown in Eq.4. Thus, the FF can be finally calculated as shown in Eq.5.

Results

This equation allows calculation of FF for CVVHF using replacement fluid for prefilter dilution. Fig. 1 shows FF versus Qrf for two example cases where Qb is 300mL/min: net UF 0mL/hour and Hct 30, and net UF 200mL/hour and Hct 45. The equation can also be easily solved for blood flow, allowing the clinician to substitute desired values for Qrf, Qufnet, and FF, and determine the required blood flow to achieve these values.

Conclusions

Prefilter dilution with replacement fluid is commonly used to reduce filter clotting in CVVHF. Risk of clotting increases for higher FF, but a method for calculation of FF in the setting of CVVHF with prefilter dilution with replacement fluid has not previously been published to our knowledge. The equation presented may facilitate quantitative clinical decision making regarding CVVHF rate settings, and decrease filter clotting.

$$FF = \frac{Q_{uf}}{Q_p} \quad (1)$$

$$Q_p = Q_b \cdot \left(1 - \frac{Hct}{100}\right) \quad (2)$$

$$Q_{uf} = Q_{ufnet} + Q_{rf} \quad (3)$$

$$Q_p = Q_{rf} + (Q_b - Q_{rf}) \cdot \left(1 - \frac{Hct}{100}\right) \quad (4)$$

$$FF = \frac{Q_{ufnet} + Q_{rf}}{Q_b \cdot \left(1 - \frac{Hct}{100}\right) + Q_{rf} \cdot \frac{Hct}{100}} \quad (5)$$

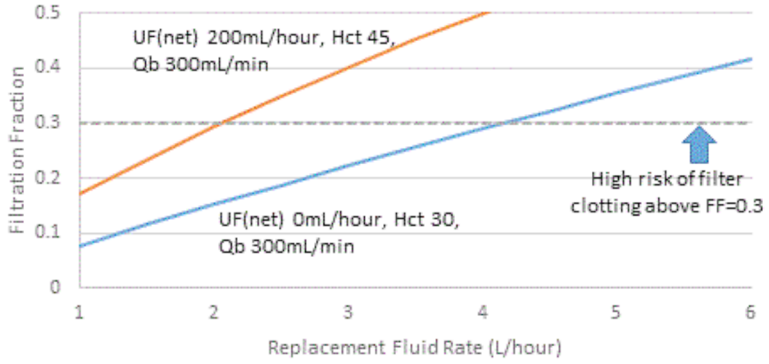
$FF, filtration\ fraction;\ Q_{uf}, ultrafiltration\ rate$

$Q_p, plasma\ flow\ rate;\ Q_b, blood\ flow\ rate$

$Q_{ufnet}, net\ ultrafiltration\ rate;\ Q_{rf}, replacement\ fluid\ flow\ rate$

$Hct, hematocrit$

Fig. 1. Filtration fraction versus replacement fluid rate for CVVHF with prefilter replacement fluid



Abstract Number 54

The role of Combination of Continuous Veno-venous Hemofiltration and Hemoperfusion in Hyperlipidemia-induced Severe Acute Pancreatitis with two patients

Han Zhang[1], Hua Gan[1]

[1]*the first affiliated hospital of Chongqing medical university, Chongqing, CN*

Aim: To assess the impact of combination of continuous veno-venous hemofiltration and hemoperfusion used in the management of two cases with hyperlipidemia-induced severe acute pancreatitis(SAP).
Patients: Two patients with hyperlipidemia-induced pancreatitis whose triglyceride levels exceed 50 mmol/L.
Treatment: Early combined ultilization of continuous veno-venous hemofiltration(CVVH) and hemoperfusion(HP) treatment, general supportive treatment and the treatment of signs and symptoms.
Case presentation: Two males were admitted to the emergency department with epigastric pain. Upon completion of series of examinations, the diagnosis of hyperlipidemia-induced severe acute pancreatitis were confirmed. The triglyceride levels were 52.40 mmol/L and 81.40 mmol/L, respectively. Based on conventional treatment, CVVH and HP were carried out. After the combined utilization of CVVH and HP, the serum level of triglycerides decreased more than 90% in less than 24 hours, thereby avoiding tissue damage. Similarly, the cholesterol, amylase and lipase level decreased dramatically in a short time. Consequently, the patients' general conditions significantly improved and their laboratory parameters virtually normalized. Both of them were discharged several days later in good health.
Conclusion: Early combined application of CVVH and HP may be a safe and feasible therapeutic modality in the treatment of hyperlipidemia-induced SAP.

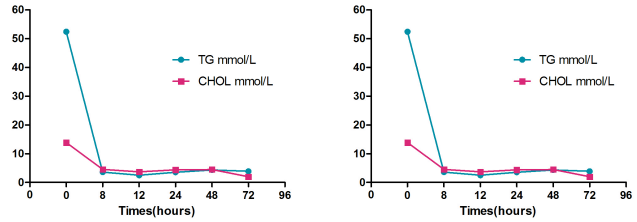


Figure 1 Case 1 The changing trendency of pancreatitis-related indicators, including triglyceride(TG), cholesterol(CHOL), lipase and amylase. Hemoperfusion(HP) and continuous veno-venous hemofiltration(CVVH) was initiated at Day1. HP was stopped at Hour 4 and CVVH was discontinued at Day 3. Normal range: TG 0.35-1.70mmol/L, CHOL 2.80-5.20mmol/L, lipase 0-300 IU/L, amylase 0-110 IU/L.

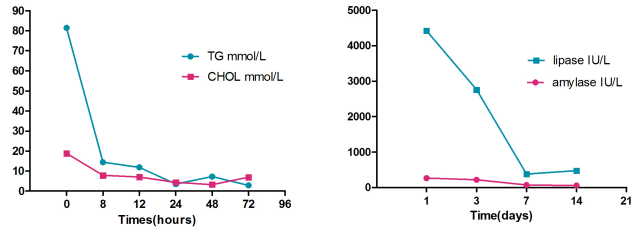


Figure 2 Case 2 The changing trendency of pancreatitis-related indicators, including triglyceride(TG), cholesterol(CHOL), lipase and amylase. Hemoperfusion(HP) and continuous veno-venous hemofiltration(CVVH) was initiated at Day1. HP was stopped at Hour 4 and CVVH was discontinued at hour 8. Normal range: TG 0.35-1.70mmol/L, CHOL 2.80-5.20mmol/L, lipase 0-300 IU/L, amylase 0-110 IU/L.

Abstract Number 55

Automated Total Fluid Management by Aquarius SW 6.02.07

Lannoy Jean-michel[1], Kelly Thomas[1], Constantini Roberto[1], Hartwig Rainer[1], Moreaux Benoit[1]

[1]*Nikkiso*

Fluid overload is one of the most frequent indications for continuous renal replacement therapies (CRRT). During therapy the patient fluid balance is maintained by the equilibrium between the fluid removed and the substitution fluid infused by the machine. This balance can be compromised if the user overrides multiple alarms without correcting the initial condition leading to hypervolemia, which could be fatal (Ronco, IJAO, 28-8, 763-764, 2005). Recently, the software of the Aquarius CRRT device (Nikkiso) incorporates a new algorithm (Patent: Total Fluid Loss Control System ECC5920), which provides a total fluid management based on the patient fluid balance.

The algorithm constantly monitors the patient fluid balance to detect deviations that may exceed the allowed limits (±50ml adult and ±20ml pediatric). If a deviation is detected, a Balance Alarm is triggered and the user is asked to check the system for possible alarm causes. When the user clears the alarm and restarts the system, the Aquarius device automatically compensates for the deviation by infusing (or removing) fluid using the substitution (or filtration) pumps. During the compensation phase, based on source of error one pump system (substitution or filtration) is activated and runs at a constant speed to reduce the patient fluid balance deviation. When the deviation is reduced to ±35ml, the compensation stops and the treatment restarts by activating all balance pumps at their programmed speed. The Aquarius system adjusts the remaining patient deviation by using the fluid regulation system that is always active during treatment. This algorithm has the advantage of allowing for fluid imbalance compensation as well as reducing the time when the patient is not treated. This increases safety and allows for a more efficacious patient clearance.

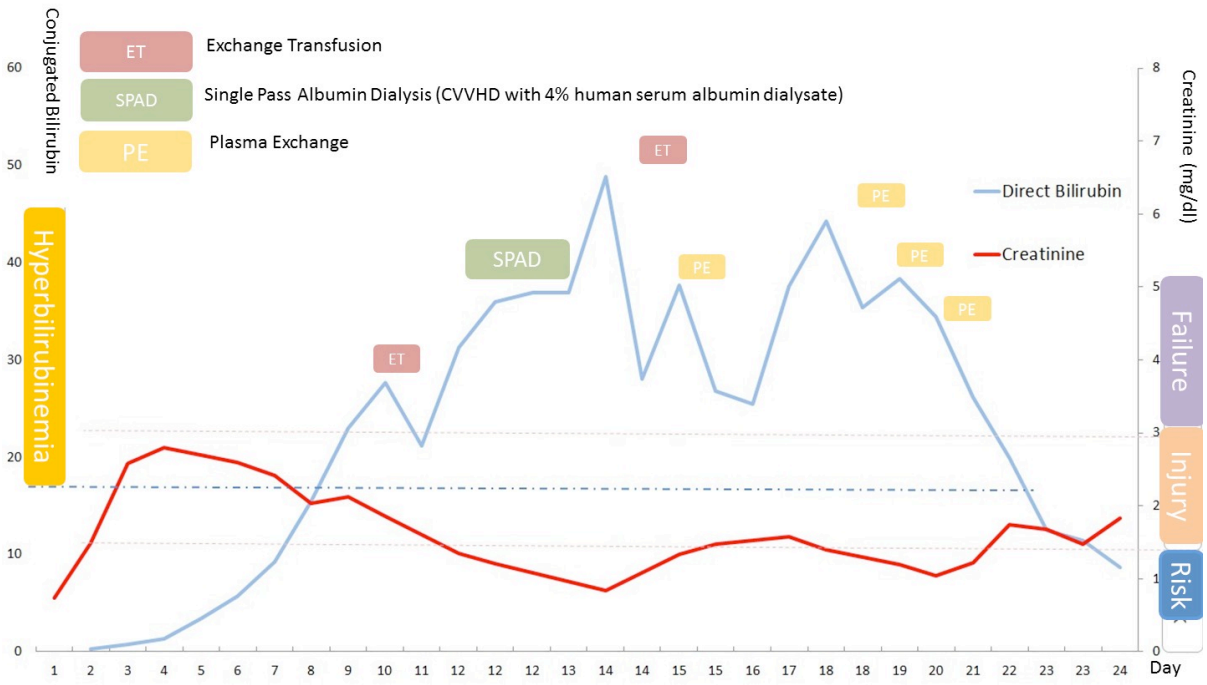
Abstract Number 56

NEONATAL ACUTE KIDNEY INJURY TREATED WITH CONTINUOUS RENAL REPLACEMENT THERAPY BY A DEDICATED MINIATURIZED TECHNOLOGY (CARPEDIEM).

Monica Zanella[1], F Garzotto[1], A Brendolan[1], F Nalesso[1], S Vedovato[2], S Bonato[2], S Di Leo[2], M Bellettato[2], C Ronco[1]

[1]*Nephrology, St. Bortolo Hospital, Vicenza, Italy,* [2]*nICU, St. Bortolo Hospital, Vicenza, Italy*

A full term female (birth weight 3165 grams) born by spontaneous vaginal delivery with vacuum extraction developed a subgaleal hemorrhage complicated by a severe hypovolemic shock and disseminated intravascular coagulation. She was intubated and mechanically ventilated.
Multi organ failure (MOF) occured including AKI with anuria, hypercreatininemia (2.8 mg/dl) and hyperkalemia (6.6 mmol/L). She received 18 transfusions of packed RBCs and fresh frozen plasma during the first 2 days of life. On day 3, baby's weight increased to 5160 g (63% fluid overload) and the pulmonary edema complicated her respiratory status.
Peritoneal dialysis was contraindicated due to hepatomegaly, melena and respiratory failure. Therefore, CRRT was undertaken using the CARPEDIEM machine.
A Dual- Lumen 4Fr catheter was placed in the femoral vein and continuous veno-venous hemofiltration was initiated.
The baby was treated by CVVH for the first two weeks until the body weight was reduced to baseline (- 2,2 Kg), creatinine decreased to 1.2 mg/dl, potassium normalized and diuresis recovered. During the following two weeks hemodialysis and hemodiafiltration were performed to correct persistent azotemia and hypercreatininemia and to manage a severe hyperbilirubinemia, due to hematoma reabsorption.
The urgent need to rapidly decrease conjugated bilirubin levels rise to 48.8 mg/dl (in order to avoid secondary cerebral damage), the hemofiltration treatment was subsequently alternated with other modalities aimed at bilirubin removal such as blood exchange, Single Pass Albumin Dialysis and plasma exchange done with CARPEDIEM machine.
A total of 401 hours of CRRT was performed without metabolic, cardiovascular or thrombotic complications.
The baby was discharged at two months of life with chronic kidney disease, but no need for RRT.
We used a new machine for CRRT CARPEDIEM to treat a case of neonatal AKI. This device can be safely used to improve the treatment and reduce the mortality of this severe condition in newborn and small infants. *figure on following page*



Abstract Number 57

Arteriovenous Access Use in End Stage Renal Disease Patients Receiving Continuous Renal Replacement Therapy

Vanya Grover[1], Adebayo Adewale[1], Sheila Donaghy[1], Mary Longobucco[1], Nand K Wadhwa[1]

[1]*Stony Brook University Hospital, Stony Brook, NY, USA*

End stage renal disease (ESRD) patients with multi-organ failure admitted to intensive care units (ICU) frequently require Continuous Renal Replacement Therapy (CRRT). We investigated the use of preexisting arteriovenous (AV) graft or fistula for vascular access to perform CRRT in these patients. The purpose of the study was to evaluate safety and efficacy of the AV access in ESRD patients requiring CRRT.

The AV access was used in twelve ESRD patients for CRRT from January 2012 to November 2013. The study population included 6 males and 6 females with a mean age of 57 years (range 32-76 years). Three patients had grafts and nine had fistulas in upper extremities respectively. The indication for CRRT included septic, hemorrhagic or cardiogenic shock. The etiology of ESRD was diabetes mellitus, hypertension and lupus nephritis. All patients were on vasopressors and eleven were intubated.

All patients had their AV access cannulated by a dialysis nurse utilizing 16 gauge plastic angio-catheters for both arterial and venous access. An ICU nurse was responsible for maintenance, and was educated to monitor the AV access on a one to one basis. Mean duration of CRRT was 19 hrs/day and total duration of therapy for the study population was 43 days. The maximal average blood flow rate was 150 ml/min. PRISMASATE BGK 4/2.5 was delivered at 500 ml/hr as a dialysate. PRISMASOL BGK 4/0 was infused at 1500 ml/hr as replacement fluid. The prescription was individualized to achieve an effluent rate of 20-25 ml/kg/hr. All patients were administered citrate for anticoagulation.

No AV access bleeding, infection or technical problems were observed. All AV accesses were functioning after the CRRT was discontinued. Five patients survived their hospital stay and received intermittent hemodialysis in the hospital prior to discharge, without complications. These patients were also followed at their outpatient hemodialysis centers. No technical problems were reported with the AV access. AV grafts or fistulas cannulated with an angio-catheter for CRRT can be used safely in the ESRD population and can obviate the need for central venous access.

Abstract Number 58

You make my blood run cold: Thermal loss of warmed replacement fluids during CRRT

Fouad T Chebib[1], Sumedh S Hoskote[1], Amy W Williams[1], Philip C Vatterott[1], Edward T Casey[1]

[1]*Mayo Clinic - Rochester, MN*

Purpose:The phenomenon of hypothermia related to continuous veno-venous hemofiltration (CVVH) is well-recognized. Hypothermia is deleterious to health, and is known to increase mortality in critically ill patients. Replacement fluid temperature and duration of its exposure to room temperature appear to be the two most important factors impacting heat transfer related to CVVH. Warming of CVVH replacement fluid prior to its use in the circuit has been thought to decrease the cooling effect exerted on patients receiving CVVH. We performed a study to evaluate the decline in temperature in CVVH replacement fluid after it had been adequately warmed.
Methods:We performed a point prevalence study on 10 consecutive patients receiving CVVH in the intensive care units with a delivered replacement fluid rate of 20-25 ml/Kg/hr. We measured the temperature of the replacement fluid in the fluid warmer located in the patient's room (warming bag), fluid running in the CVVH machine (active bag), the ambient surroundings and the patient's temperature. We recorded the time elapsed since the warming bag was placed in the fluid warmer and the time elapsed since the active bag was placed in the CVVH circuit. We estimated the volume remaining in the active bag based on the replacement fluid flow rate.
Results:The temperature of the replacement fluids in a fluid warmer reaches approximately 100 ˚F and stabilizes in about 120-200 minutes (Fig.1). The active bag loses heat and almost reaches room temperature in 200 minutes, losing 26 ˚F in the process (Fig.2). Similarly, as time elapses, the difference between temperatures in the active fluid bag and the patient also increases, reaching a difference of 16-20˚F after 120 minutes (Fig.3). Changes in temperature were correlated strongly with time in all comparisons.
Conclusions:Warming of CVVH replacement fluid prior to their use during CVVH only has a transient effect on maintaining a physiologic temperature in the replacement fluid. Once the bag is attached to the CVVH circuit, heat exchange occurs quickly with ambient air leading to a significant drop in temperature over the next several hours.This loss of heat probably contributes significantly to the hypothermia associated with CVVH in critically ill patients. Aside from passive external warming, few treatments exist for managing CVVH-associated hypothermia. Further research is needed to develop innovative methods for reducing cold stress and hypothermia associated with CVVH.

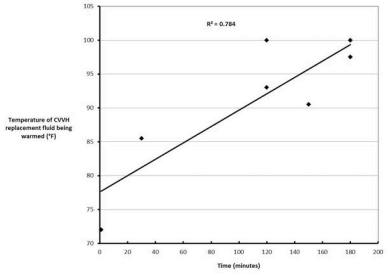


Figure 1: Temperature of replacement fluids in the warming blanket in relation to time elapsed during warming

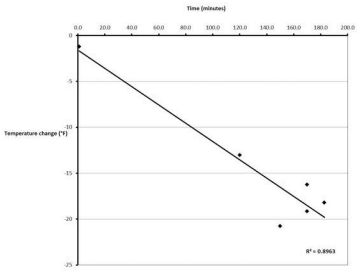


Figure 3: Difference in temperatures between the delivered fluids and the patient average temperature in relation to time elapsed on CVVH using the same bag of replacement fluids.

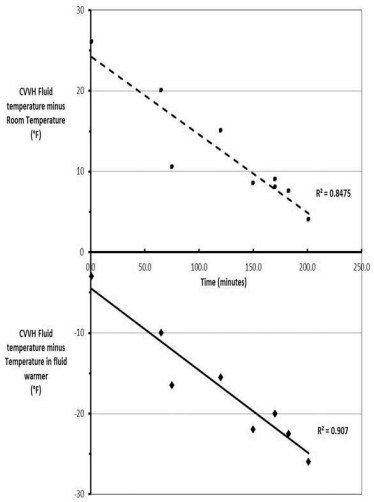


Figure 2: Upper panel – Pre-warmed CVVH fluid temperature approaches ambient temperature over time. Lower panel – Heat lost by the CVVH fluid over time after being pre-warmed.

Abstract Number 59

Piperacillin-Tazobactam Concentrations in an In-Vitro Model of CVVH: Their Drastic Reduction and an Innovative Modality of Administration to Obtain Costant Serum Levels.

Michele Ferrannini[1], Alessia Centi[1], Massimo Smeriglio[1], Pasquale Massa[1], Stella Caramiello[1], Paola Tatangelo[1], Angela Lombardo[1], Maria Grazia Sergi[1], Damiano Di Franco[1], Roberto Palumbo[1]

[1] *"St Eugenio" Hosp. Nephrology and Dialysis Unit - Rome - Italy*

Background: Critically ill patients often need CRRT and antibiotic therapy. Piperacillin-Tazobactam (Pip-Tzb) are antibiotics frequently used in ICU but they are eliminated by CRRT and at the present a consensus about their correct doses is still lacking. Aims: to evaluate Pip-Tzb removal mechanisms (clearances and eventual absorption) during an in-vitro single pool model of Continuous-Veno-Venous-Hemofiltration (CVVH); (2) to keep constant concentrations of Pip-Tzb during an in-vitro model of CVVH, testing a new simple way of Pip-Tzb administration, using the reinfusion bags of the CVVH system.
Materials and Methods. A CVVH system was used to obtain an in-vitro single pool model. We tested, in different CVVH sessions, as a Protein-Free-Solution added with Pip-Tzb (4gr - 0.5 gr respectively), as 1L of free frozen plasma (FFP) added with 350 and 43.75 mg of Pip-Tzb. Before starting CVVH, we tested a possible adsorption of Pip-Tzb on fibers of dialyzer as with PFS as with FFP. Then, to test drug removal from solutions, we started CVVH. Sieving Coefficients (SC) and Clearances were calculated. Then, we tested the same models adding in every fluid replacement bags 80 mcg/mL and 10 mcg/mL of Pip-Tzb respectively, miming their minimal inhibitory concentrations (MIC).
Results. (1) We did not observe any considerable absorption mechanism using FPS, but with FFP we observed that free and total Pip-Tzb concentrations decreased during the first minutes. (2) During CVVH with FPS the Pip-Tzb concentrations decreased of 70% and 54.8% respectively in 2 hours; the SCs of Pip-Tzb were about 1.0 and clearances were 1500 ml/h and 1482 ml/h respectively. Similar data we obtained with FFP: after two hours the free and total Pip concentrations decreased from 266 and 318 mcg/ml to 22 and 33 mcg/ml respectively, becoming undetectable in the rest of time; Tzb free and total concentrations decreased from 42 and 52 mcg/ml to 4 and 6 mcg/ml respectively, becoming undetectable in the rest of time. (3) About CVVH with Pip-Tzb in reinfusion bags we achieved constant concentrations of Pip-Tzb above their MIC during all the time (8 hours).
Conclusion: Pip-Tzb are rapidly cleared with a risk of inadequate dosages in patients undergoing to CRRT. In an in-vitromodel, adding Pip-Tzb in the reinfusion bags we can obtain a “plateau” of concentrations of drugs with SC 1. We judge this system theoretically solid and results promising, but need a clinical trial.

RRT APPLICATIONS AND TARGETED INTERVENTION

Abstract Number 60

Using High Bicarbonate Concentration Replacement Solution in CVVH is Associated with Higher Mortality: a Retrospective Cohort Study

Gina M Iacovella[1], Robert C Albright[1], Abbasali Akhoundi[1], Pramod K Guru[1], Joshua S Botdorf[l], Andrea B Braun[1], Charat Thongprayoon[1], Kianoush B Kashani[1]

[1]*Mayo Clinic*

Background: Acute kidney injury (AKI) is a common complication encountered in the intensive care unit (ICU) and at times, requires initiation of renal replacement therapy (RRT). We hypothesized that utilizing high bicarbonate (HCO3) concentration replacement solution in continuous veno-venous hemofiltration (CVVH) is associated with higher mortality after adjustment for severity of illness and comorbid conditions. We defined a high HCO3 concentration containing 32mM/L and a low HCO3 concentration containing 22mM/L. To our knowledge, this is the first report of high HCO3 CVVH solution association with

increased mortality.
Methods: We performed a retrospective, observational study at a single tertiary care center from 12/09/2006-12/31/2009 with follow-up for a total of 68 months. A cohort of 301 consecutive adult ICU admissions were identified based on age>18 years and Stage III AKI via AKIN criteria requiring CVVH. Exclusion criteria were age <18 years old, pregnant patients, prisoners, patients on either intermittent hemodialysis or peritoneal dialysis prior to hospitalization, patients who received other forms of continuous RRT, and patients that received mixed high and low HCO3 replacement solutions.
Results: Of the 301 patients, 74 (24.6%) were initiated on CVVH using a high HCO3 solution and 227 (75.4%) on a low HCO3 solution. The most common cause of AKI was ATN, 48 (64.9%) in the high and 165 (72.7%) in the low HCO3 solutions. The total number of deaths within each group were 58 (78.4%) in the high HCO3 solution vs. 165 (72.4%) in the low. When mortality results were adjusted for age, gender, BMI, APACHE 3 score, SOFA score at day #1, and Charlson score, there was an increase at both 28-days ($p<0.05$) and 68 months ($p<0.005$) between the high vs. low HCO3 solutions. At the time of CVVH initiation, patients on the high HCO3 solution had higher APACHE 3 scores ($p<0.001$), higher Norepinephrine requirements ($p<0.01$), higher lactate ($p<0.0005$), lower pH ($p<0.0001$), and lower albumin ($p<0.05$). The high HCO3 group had a higher incidence of intra-dialytic hypotension 1-hour following initiation of treatment ($p<0.005$).
Conclusion: Our data showed there is a strong association between using high HCO3 solution and mortality independent of higher severity of illness, comorbid conditions, and cause of ATN. Further prospective studies are needed to evaluate the role of high HCO3 solution as an individual risk factor for mortality.

Abstract Number 61

Seven cases of refractory Kawasaki disease treated with plasma exchange therapy

Mariko Sawada[1], Kayo Ogino[1], Tomohiro Hayashi[1], Masumi Saito[2], Kenji Waki[1], Yasunori Ueda[3], Yoshio Arakaki[1]

[1]Department of Pediatrics, Kurashiki Central Hospital, [2]Department of Clinical Engineering, Kurashiki Central Hospital, [3]Department of Hematology, Kurashiki Central Hospital

Objective
Kawasaki disease (KD) is one of the most common childhood vasculitis in Japan. The goal of treatment in KD is to reduce inflammation and prevent the formation of coronary aneurysms. Intravenous gammaglobulin therapy (IVIG) is recommended as the first-line treatment. However, some cases are refractory to IVIG, and their coronary artery may show dilatation. The cause of KD remains unknown. Some papers report that it is important to reduce levels of inflammatory cytokines in plasma for preventing coronary arteritis and the resultant coronary aneurysms. We aimed to determine if removal of inflammatory cytokines from plasma with plasma exchange (PE) therapy can inhibit coronary lesions.
Patients
Seven male patients (age range, 7 months to 13 years; body weight, 8–43 kg) with refractory KD did not show improvement of fever and levels of inflammatory markers after IVIG (3–7 g/kg). They had cardiovascular manifestations such as mild dilatation of the coronary artery, pericardial fluid, valve regurgitation, and cardiac hypofunction. Therefore, they were treated with PE 10–18 days after the onset of refractory KD. They did not have any other diseases.
Methods
PE was performed in 3–6 sessions with 3–5% albumin per 1–2 plasma volumes within 2 hours per session. Vascular access was obtained by inserting 6.5–10 Fr urokinase-coated double lumen catheters in the femoral veins. The blood flow was 2–4 mL/kg/min. The anticoagulant used was heparin.
Results
In all cases, after PE, there was rapid improvement of fever and erythema and decrease in inflammatory marker levels (CRP) and WBC and neutrophil counts. No serious complications were observed.
The prognosis of cardiovascular manifestations after 1 month was observed in 2 patients with persistent coronary dilatation and 1 patient with giant coronary aneurysm. After 1 year, the coronary artery dilatations regressed spontaneously in both patients, whereas the giant coronary aneurysm persisted in 1 patient.
Conclusions
We could perform safe and effective PE treatment in infants and children with cardiac hypofunction. Four of 7 patients were effectively treated with PE to prevent the progression of coronary artery lesions; 2 of them showed regression of dilation in the coronary arteries within 1 year. Only 1 patient showed a coronary aneurysm. We obtained a good prognosis for the coronary artery in patients with refractory KD.

Abstract Number 62

Therapeutic Plasma Exchange in Pediatric Fulminant Liver Failure

Amy S Arrington[1], Moreshwar S Desai[1], Poyyapakkam R Srivaths[1], Jun Teruya[1], Shiu-Ki Hui[1], John A Goss[1], Annabelle N Chua[1], Ayse A Arikan[1]

[1]*Baylor College of Medicine / Texas Children's Hospital*

Pediatric patients with acute and acute-on-chronic fulminant liver failure (FLF) develop life-threatening complications, including refractory coagulopathies, hepatic encephalopathy, cardiovascular collapse, multi-organ failure and death. Therapies for patients awaiting transplant are merely supportive, and include large volumes of blood products to correct coagulopathy, resulting in volume and protein overload and citrate toxicity. Therapeutic plasma exchange (TPE) allows for improved management and prevention of these complications while correcting coagulopathy, and can be done in tandem with continuous renal replacement therapy (CRRT). There are no published pediatric studies describing the safety or efficacy of TPE in FLF. Methods: Charts of all liver failure patients from 2012-2013 at Texas Children's Hospital who received TPE for hepatic encephalopathy and /or severe coagulopathy (n=15) were retrospectively reviewed. TPE was performed by replacing 1.5 total plasma volume with fresh frozen plasma, and anticoagulation was regional with citrate. A protocol for TPE in patients with FLF was used for all patients in 2013 (n = 11), and included 5 daily TPE treatments, followed by every other day TPE until transplant or death. Prior to this protocol, TPE was used randomly on a physician- directed basis. Data: Over 2 years, 15 patients with FHF were treated with TPE. The number of treatments ranged from 1 to 16 (5 per patient, median). TPE was done in tandem with CRRT in 11/15 patients; 9 patients experienced citrate lock, which improved by increasing calcium chloride. The most common side effect was hypotension requiring inotropic support (73%), and bleeding from catheter sites (67%). No treatment interruption was necessary secondary to hemodynamic instability, even in patients on multiple vasoactive agents. No direct infectious complications or deaths were associated with TPE. In the 11 patients subject to the 2013 protocol, 5 were successfully bridged to liver transplantation, and 1 had spontaneous resolution of disease. Conclusions: These data demonstrate the safety of TPE in children with FHF. Advantages include control of refractory coagulopathy and encephalopathy. We speculate that TPE assists in removal of circulating toxins, bile acids, and inflammatory mediators leading to severe end-organ dysfunction. These benefits allow for longer survival while waiting for liver transplant, and potentially improve post-operative survival.

Abstract Number 63

The Use of a Phosphate-Containing Dialysis Fluid Reduces Episodes of Hypophosphatemia in CRRT Patients

Ola Carlsson[1], Marcus Broman[2], Bengt Klarin[2], Gabriela Godaly[3]

[1]*Gambro Lundia AB, Lund, Sweden,* [2]*Department of Anaesthesiology and Intensive Care, Skane University Hospital, Lund, Sweden,* [3]*Department of Microbiology, Immunology and Glycobiology, Lund University, Lund, Sweden*

Background:
Electrolyte disturbances are common in CRRT patients. Routine blood sampling is used to restore physiological levels of the electrolytes, but this procedure is troublesome and laborious. Phosphate has long been a neglected ion, but episodes of hypophosphatemia are connected to several complications such as cardiac arrhythmias, seizures, and hemolysis. However, previous pilot clinical study testing phosphate-containing dialysis and replacement fluids indicated promising results regarding hypophosphatemia and plasma phosphate stabilization. The present retrospective study was initiated to investigate the effects of phosphate-containing CRRT fluids on ion homeostasis in a larger patient material compared to previous studies.

Methods:
In total 112 patients treated with CRRT at the University Hospital in Lund, Sweden were retrospectively included in the study. The control group (n=36) was treated with Hemosol B0 as dialysis and replacement fluid, while the study group (n=76) received Phoxilium as dialysis fluid and Hemosol B0 as replacement fluid. Data for the entire dialysis treatment were collected and analyzed. Patients were treated according to current standard treatment at the clinic.

Results:
Treatment with conventional fluids lead to hypophosphatemia (<0.7 mM) during 17% of the treatment days in the control group, compared to only in 10% in the study group, (p=0.027). There was no difference in hypomagnesemia but the magnesium substitution was four times higher in the control group compared to the study group (16.8±2.8 vs. 4.9±1.2 mmol per treatment, p<0.001). There were indications that patients in the study group were more severely ill, as indicated by higher expected mortality rate as well as a significantly lower blood pressure throughout the treatment period. Acid-base balance as well as potassium levels were not different between the groups.

Conclusions:
We could confirm that the phosphate-containing dialysis fluid reduces the episodes of hypophosphatemia in CRRT patients. The reduction in magnesium supplementation indicates that slightly higher concentration of magnesium in the fluids is beneficial for the patients. Thus, the use of Phoxilium is a simple and safe way to reduce the incidence of hypophosphatemia that might reduce complications in the long-term and improve patient outcome during CRRT. It would also be interesting in the future to evaluate if Phoxilium can be used as replacement fluid.

	Phoxilium (mmol/l)	Hemosol B0 (mmol/l)
Bicarbonate	32	30
Calcium	1.75	1.25
Chloride	109.5	115.9
Lactate	3	0
Magnesium	0.5	0.6
Phosphate	0	1.2
Potassium	0	4
Sodium	140	140

Abstract Number 64

'Locking' Untunneled Central Venous Catheters in Critically Ill ICU patients on RRT to Prevent CRBSI

ANIL K SAXENA[1], CHANDRA MAULI JHA[1], AYMAN K AL MADANI[1], ABOU CHACRA SAMARA[2], MOHAMMED CHAABAN[2], DASTOOR D HORMUZDIAR[1]

[1]MAFRAQ HOSPITAL, [2]TAWAM HOSPITAL, AL AIN, ABU DHABI, UAE

Catheter related bloodstream infections (CRBSIs) are common among patients undergoing renal replacement therapy (RRT) through untunneled catheters (UTC) in intensive care units; placing them at a greater risk of CRBSI related morbidity and mortality. Several randomized controlled trials have shown that intraluminal placement of antimicrobial lock (AML) solutions – Taurolock, Cefazolin, Cefotaxime in combination with anticoagulants (heparin / citrate) improve tunneled catheters (TC) outcomes among stable Outpatient HD patients. However, the role of AML has not been sufficiently investigated among patients undergoing RRT through UTC in ICU.
Present study was designed to investigate the role of AML in prevention of CRBSI and UTC outcomes in critically ill patients on RRT in ICU.
This prospective Investigation was carried out in medical and surgical ICUs of Mafraq Hospital (SEHA Group of Hospitals), Abu Dhabi, UAE. Of 249 patients admitted to ICU with AKI- 117 were identified to receive RRT (HD/ SLED/ CRRT) during the study period (August 2010 to July 2012). Subjects were assigned to - Group I: n =58 (Control, locked with standard Heparin 5000 U/ mL) and, Group II: n =59(locked with Taurolock®).
All the adults (≥18 years) on RRT (HD/ SLED/RRT) with UTC in ICU were included in the study. Subjects with clinically evident infection and those having progressed to ESRD were excluded from the study.
Demographic data and baseline characteristics in terms of age, gender, type, frequency & duration of RRT, (days), type (femoral, internal jugular), & duration (Catheter-days) of UTC S, Serum iron, ferritin, transferrin saturation (T. Sat), proportions of diabetic and elderly subjects besides the possible underlying etiology of the AKI and other organ involvement (lung, liver, heart, Brain), were recorded.

Catheter thrombosis and CRBSI rates between two groups were recorded and statistically compared.
Significantly lower (p=0.023) CRBSI and related mortality rates were observed in group II (locked with Taurolock ®) compared to Group I (Control, locked with standard Heparin). However, patients in the Taurolock group (Group II) recorded significantly higher catheter thrombosis rates (p-0.041) than the heparin locked group (Group I).
Intraluminal placement of Taurolock ® reduces CRBSI and related mortality among critically ill patients with AKI undergoing RRT in ICU. However, it is associated with higher catheter dysfunction due to thrombosis.

Abstract Number 65

Critically Ill Pediatric Patients on Continuous Renal Replacement Therapy Fail to Meet Nutrition Goals after Therapy Initiation

Molly W Vega[1], Carolyn Smith[1], Mary N Watson[1], Alyssa Riley[2], Helen Currier[1], Ayse Akcan Arikan [2]

[1]Texas Children's Hospital, [2]Baylor College of Medicine

Protein and energy underfeeding is very common in critically ill children and is exacerbated in patients with acute kidney injury (AKI). Positive fluid balance is an increasingly well recognized morbidity and mortality risk factor in children. Conservative management of oligoanuric AKI requires fluid restriction, often placing significant confines on delivery of nutrition. In our institution, ability to provide adequate nutrition is a frequent indication for starting continuous renal replacement therapy in our pediatric intensive care unit (PICU). However, habitual practices of restricting protein provision in AKI and gradually increasing caloric intake even with parenteral nutrition still are very common. We hypothesized that despite recent PICU-wide education incentives aiming to optimize nutrition intake, patients on CRRT still are underfed. We retrospectively reviewed the charts of patients receiving CRRT in our PICU over the last 6 months. Indications for treatment were clearance and fluid removal. Patients with inborn errors of metabolism who have altered nutritional requirements were excluded. There were 25 patients, ages ranging between newborn to 18 years of age. With the exception of two patients who received modified CRRT through an extracorporeal circuit, all other patients received CRRT via dedicated stand-alone machines in the continuous venovenous hemodiafiltration mode (CVVHDF). We reviewed the patients' energy and protein intake (enteral and parenteral combined) within 48 hours of starting CRRT and compared the nutritional intake to institutional recommendations. Only 36% of the cohort reached both protein and energy goals within 48 hours. 44% of the patients were receiving adequate energy intake by the end of 48 hours compared to only 40% of the patients who were receiving adequate protein prescription. These preliminary data indicate that critically ill pediatric patients receiving CRRT are at high risk of underfeeding. Further studies investigating how nutritional practices evolve over time and identification of barriers to adequate prescription are needed.

Abstract Number 66

Protective Effect of Coupled Plasma-Filtration Adsorption (CPFA) on Bile-associated Cast Nephropathy and Tubular Injury through Direct Adsorption of Bilirubin and Liver-type Fatty Acid Binding Protein

Vincenzo Cantaluppi[1], Davide Medica[1], Alessandro D Quercia[1], Sergio Dellepiane[1], Silvia Ferrario[1], Marialuisa Caiazzo[2], Luigi Biancone[1]

[1]Nephrology, Dialysis and Kidney Transplantation Unit, University of Torino, [2]Scientific Affairs, Bellco srl, Mirandola (MO), Italy

Background and aim of the study
Bile-associated cast formation and tubular injury are possible causes of acute kidney injury (AKI) during liver dysfunction. The mechanisms of bilirubin-associated AKI are due to cast formation and tubular cell apoptosis. Liver-type Fatty Acid Binding Protein (L-FABP) is a 15 KDa peptide belonging to free fatty acid family able to bind hydrophobic molecules including bilirubin. During liver failure, the increase of L-FABP plasma levels enhances bilirubin uptake and consequent damage of tubular cells through a megalin-dependent pathway.

We investigated the protective role of Coupled Plasma Filtration Adsorption (CPFA) on bile cast nephropathy through L-FABP and bilirubin resin adsorption.
Methods
We reported the case of a kidney transplant patient who developed sepsis, AKI and liver dysfunction treated by CPFA. We evaluated plasma levels of bilirubin and L-FABP. Renal biopsies, urine sediment and NGAL were performed at different time points. In vitro, we tested: 1) static and dynamic adsorption of L-FABP to polystyrene resin; 2) pro-apoptotic effect (TUNEL) of patient's plasma drawn before and after CPFA on human tubular cells: the role of L-FABP was confirmed in tubular cells engineered to knock-down megalin by siRNA.
Results
A 50-year-old man was subjected to kidney transplantation with slow recovery of graft function. Kidney biopsy revealed acute tubulo-interstitial and vascular rejection treated with thymoglobulin. He then developed septic shock for Legionella with multiple organ failure (serum creatinine 5.2 mg/dl and oliguria requiring dialysis; bilirubin 42 mg/dl with liver biopsy showing marked cholestasis; plasma L-FABP 42 ng/ml). Urine analysis showed the presence of tubular cells and intense positivity for bilirubin: urine NGAL level was 356 ng/ml. A new kidney biopsy showing bile cast nephropathy was performed. After CPFA was started, we observed an increase of urine output, a decrease of bilirubin (<15 mg/dl), L-FABP (7 ng/ml) and urine NGAL (72 ng/ml). In vitro, the polystyrene resin efficiently adsorbed L-FABP. After CPFA, the pro-apoptotic activity of patient's plasma on tubular cells was significantly reduced. In addition, plasma-induced tubular apoptosis was dependent on the presence of megalin, the L-FABP receptor.
Conclusions
CPFA may have a protective role in bile-associated cast nephropathy and tubular apoptosis through the direct adsorption of bilirubin and L-FABP to the synthetic polystyrene resin.

NEW TECHNOLOGY

Abstract Number 67

Continuous veno-venous hemofiltration treatment for severe acute myocarditis mainly manifesting in ventricular tachycardia

Xinli Cao[1], Han Zhang[2], Hua Gan[2]

[1]ChongQing Medical University,ChongQing,ChongQing,China, [2]the First Affiliated Hospital of ChongQing Medical University,ChongQing,ChongQing,China

Myocarditis mainly manifesting in ventricular tachycardia(VT) is rare but related to poor prognosis.The therapy of myocarditis and VT in acute myocarditis haven't reached a definitive conclusion.We present a case in a previously healthy 40-year-old woman who appeared as palpitation and syncope after chills and fever for 5 days. Her physical examination revealed a pulse rate of 102 beats/min,blood pressure of 83/59mmHg,electrocardiogram showed sinus rhythm with 0.1~ 0.4mv ST-segment elevation in leads V1~3. Results of laboratory analyses were myoglobin 356.3ug/L, troponinT 5.26ug/L. But coronary arteriography within 3 hours of admission did not show any abnormalities.Subsequently she appeared as recurrent VT complicated by Adams-Stokes syndrome,sustained hypotension,myocardial infarction-like change in electrocardiogram, diagnosed as acute severe myocarditis did not improve by repeat electric defibrillation,conventional anti-arrhythmic drugs,anti-shock therapy,elevation of blood pressure and intra-aortic balloon pump(IABP),but got remarkable curative effect after the treatment of continuous veno-venous hemofiltration(CVVH),Since CVVH(prismaflex, hemofilter AN69,area 0.9m2,blood flow 80ml/min, ultrafiltrated volume 50ml/h, replaced blood flow 3000ml/min) started, her sinus rynthm was maintained, heart rate gradually decreased to 70~80/min,the elevated ST-segment fell back to normal in lead V1~3, blood pressure remained above 100/50mmHg gradually. Then the blood flow raised to 150ml/min and ultrafiltrated volume increased. During the 50 hours treatment of CVVH, filter was changed for 6 times and ultrafiltration volum had totaled of 3500ml. This is the first report about CVVH to treat the severe myocarditis presenting with VT.

Abstract Number 68

Use of Molecular Adsorbent Recirculating System (MARS) Therapy in children.

Scott A Ludes[1], Francisco Flores[2], Kristina Burger[1]

[1]All Children's Hospital, [2]Division of Pediatric Nephrology, University of South Florida, Morsani College of Medicine, Tampa FL

Purpose: Molecular Adsorbent Recirculating System (MARS®) is an extracorporeal detoxification system that uses an albumin-based dialysis solution to selectively remove albumin-bound and water-soluble molecules. MARS® is used for the management of drug overdose, poisoning, hepatic encephalopathy. MARS® therapy is not widely available to pediatric patients and this report is our center's initial experience and patient outcomes. Method: This study is an Institutional Review Board approved retrospective case review of two pediatric patients (pts) who received MARS® therapy at All Children's Hospital. Patient #1 was a 17-year-old male with Methotrexate (MTX) intoxication and Acute Kidney Injury (AKI), after receiving therapy for Acute Lymphocytic Leukemia. Patient #2 was a 5-year-old girl with Autosomal Recessive Polycystic Kidney Disease, status post liver and kidney transplant who developed multi-organ dysfunction syndrome, AKI and acute liver failure, secondary to septic shock. MARS® therapy was provided to both patients for three consecutive days in tandem with Continuous Renal Replacement Therapy (CRRT) using the Gambro® PRISMA and MARS® circuits. Between MARS® treatments, pts received CRRT for the management of AKI. Results: In pt #1, initial high MTX level was reduced by CRRT (222 to 1.97 umol/L) with a rebound after temporarily stopping CRRT. The addition of MARS® resulted in a further 84% MTX reduction (2.19 to 0.36 umol/L). Pt's creatinine improved from 2.34 to 0.74 mg/dL by day three of MARS®. Pt's recovery of renal function resulted in ongoing reduction of MTX level to 0.08 umol/L at time of hospital discharge. Pt did not experience any complications related to high MTX levels. In pt #2, MARS® was started on day one of admission and resulted in an 88% reduction in Aspartate Aminotransferase (AST)[12505 IU/L to 744 IU/L] and a 37% reduction in Alanine Aminotransferase (ALT)[6408 IU/L to 4030 IU/L] by the day following last MARS® treatment. ALT and AST levels continued to improve off MARS® and returned to pt's baseline ALT of 68 IU/L and AST of 36 IU/L by day 21 post MARS®. Conclusions: MARS® therapy was successfully implemented in our center with no clinical complications. We consider MARS® therapy a viable and important supportive therapy for children with life threatening intoxications and liver dysfunction. As with other forms of extracorporeal support therapies, early initiation of MARS® resulted in improved outcomes.

Abstract Number 69

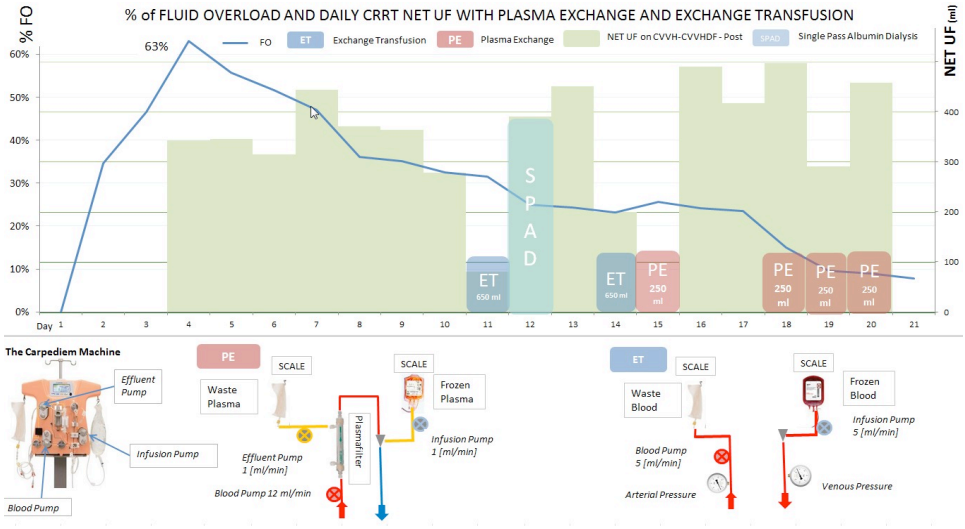
New technology for: CRRT, Plasma Exchange and Blood Exchange in Infants

Francesco Garzotto[1], M Zanella[1], A Brendolan[1], S Vedovato[2], V Di Leo[2], S Bonato[2], M Belletato[1], F Chiarenza[3], C Ronco[1]

[1]Nephrology, St. Bortolo Hospital, Vicenza, Italy, [2]nICU, St. Bortolo Hospital, Vicenza, Italy, [3]Pediatric Surgery, St. Bortolo Hospital, Vicenza, Italy

Background: CRRT is becoming the treatment of choice to support critical pediatric patients with AKI and fluid overload(FO).This therapy is usually performed with machines designed for adults thus necessarily with an over-dimensioned catheter. This is a case of a newborn with severe FO who received CRRT primarly to remove fluid excess
Objective: Patient 3.165 Kg was a 39 gestational week female,born with dystocic delivery and Apgard score 2-5-5(1-5-10m).Patient was immediately intubated and transferred to the pICU with hemorrhagic shock and MOFS due to subgaleal hemorrhage.A total of 18 transfusions of blood product was done during the first 48h.Oligoanuric despite continuous diuretic infusion and the need of fluid intake to preserve the hemodynamic,result in a 63%FO
Design/Methods: CVVH was performed, PRISM2=32, using a double lumen 4FR(2in) catheter placed in the femoral vein.A total of 401 hours of CRRT was done.Mean Blood flow was 11±2ml/m and Net UF 20.2± 5.6ml/h.Infusion was setting to maintain the Filtration Fraction<20%. Hyperbilirubinemia due to hematoma adsorption,suggests the need of SPAD.We also perform,4 plasma exchange PE and 1 exchange transfusion ET done successfully with our development of these new tecniques on the CARPEDIEM machines.
Results: For the first time we were able to use a small and adequate double lumen catheter to perform CRRT in newborn with excellent circuit survival 18.1±3.7.
Hyperbilirubinemia has olso been fell with a combined strategy of PE, SPAD and ET using the same technology.
No adverse event (ie hypotension) was observed during treatments,neither connection and conduction.

Estubated after 3 weeks patient was discharged to pediatric division after 38d
Conclusions: New CRRT,PE,ET device is safe and effective to treat newborn with small and adequate catheter not only for CRRT bu also with other extracorporeal treatments.



Abstract Number 71

AKI Electronic Alert

Emma Stevenson[1], Saba Hafeez[1], Freya Baird[1], Rosa S Chaparro[1], Suki Sankaralingam[1], Jason Button[1], Anthony Chan[1], Sumith Abeygunasekara[1], Galil Ali[1]

[1]*Broomfield Hospital*

Background: Acute kidney injury (AKI) occurs in 5-20% of all hospital admissions in the United Kingdom. It is responsible for increase in mortality and morbidity, length of stays, admissions to intensive care and cost to the National Health Service. According to the National Confidential Enquiry into Patient Outcome and Death, AKI was avoidable in 20-30% of cases, and that with better management, up to 12,000 lives could be saved each year. Poor standard of care was identified due to delay and even failure to recognise AKI. To improve early AKI detection, an electronic alert system was established at Mid Essex Hospital Trust. This e-Alert would be triggered when there is a delta rise in serum creatinineof more than 26 µmol/L from the patient's the lowest baseline value in the preceding 6 months. An advisory warning of potential diagnosis of AKI is made on the pathology reporting system and a link to the Hospital AKI Management Guideline is referred to.

Method: A retrospective audit was carried out to ascertain if the e-Alert triggers are acknowledged by doctors and appropriate care as per AKI Guideline initiated. 103 patients triggered the e-Alert for AKI in a 2-week period in November 2013, and of these 86 case notes were available for review and data collected using a standardised proforma.

Results: Out of 86 cases, only 29% had a diagnosis of AKI acknowledged based on either a documented diagnosis of AKI in the case notes or a change in management. 95% of these patients had their management reviewed in line with Hospital AKI Guideline. These were prescription of intravenous fluids, withdrawal of nephrotoxic medications or organising renal ultrasound. Of the patients discharged at the end of the audit period, only 9% had diagnosis of AKI stated in the discharge letters to the patients' general practitioner. Only 2 patients required ITU admission or haemodialysis therapy. 4 patients who triggered the e-Alert were discharged without repeat renal function tests.

Conclusion: In this audit only a third of the triggered e-Alerts were acknowledged by the medical team of the patients triggering the alert. The pick-up rate is rather low which could have adverse effects on the patient's outcome. There should be greater awareness made to all doctors in this Hospital regarding the use of e-Alert and the need for action following its trigger.

Abstract Number 72

Comparison of central venous pressure with cardiac output measured by non-invasive cardiac output monitoring in patients with continuous renal replacement therapy

Joon-Seok Oh[1], Jin-Ho Lee[1], Seong-Min Kim[1], Yong-Hun Sin[1], Joong-Kyung Kim[1], Mi-Sun Kim[2]

[1]Bong Seng Memorial Hospital, [2]MH Yonsei Hospital

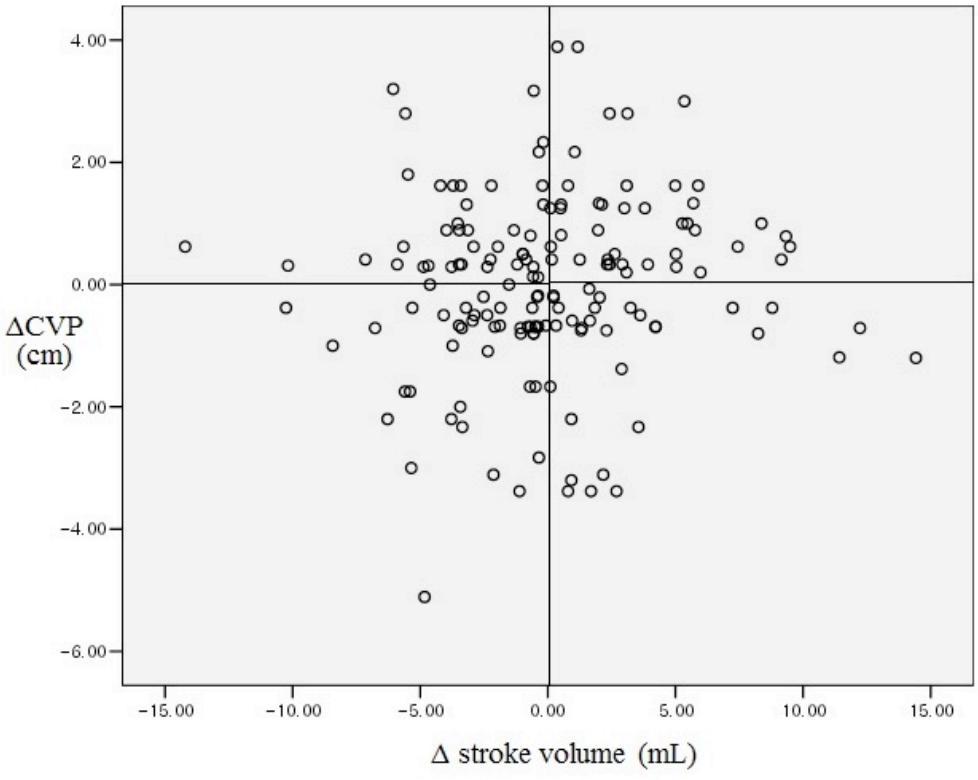
Introduction: Patients who receiving continuous renal replacement therapy (CRRT) due to their critical illnesses can be hemodynamically unstable because their peripheral resistance and blood volume changes frequently. Cardiac output (CO) is a key variable when describing and treating the cardiovascular system. Thermodilution via a pulmonary artery catheter is the most frequently used method, but it lacks accuracy. Non-invasive cardiac output monitoring (NICOM) measures CO based on chest bioreactance. Validated data of NICOM in patients with CRRT are lacking. So we compared central venous pressure (CVP) with cardiac output monitored via NICOM system in patients with CRRT.

Methods: Stroke volume (SV) values using NICOM were recorded in patients with CRRT and CVP values were measured at the same time. The difference between measured and average values of CVP (_CVP) and SV (_SV) were calculated in each subject, because CVP values may be different depending on the person who measured. Correlation analysis was performed _SV with and _CVP.

.

Results: Twenty five subjects (12 males and 13 females; mean age, 70.3 ± 8.6 years) were enrolled. And mean treatment duration of CRRT were 6.3 ± 6.5 days. Seventeen of subjects were treated with inotropic agent and 11 of them were treated with mechanical ventilation. The SV and CVP values of subjects' were measured 157 times. There were poor correlation with _SV and _CVP (R = 0.07, P = 0.37, Figure 1).

Conclusions: Stroke volume measured by NICOM and CVP showed poor correlation. NICOM may not be effective as non-invasive method for circulating volume monitoring in patients with CRRT.



Abstract Number 73

Extracorporeal Mesenchymal Stromal Cell Therapy for Critical Care

Biju Parekkadan[1], Jemma Taipan[2], Alexis Rodriguez[2], Timothy Lyford[2], Arno Tilles[2]

[1]Harvard Medical School, Boston, MA, USA, [2]Sentien Biotechnologies, Inc., Medford, MA, USA

Extracorporeal therapy has been a traditional approach to correct metabolite and fluid abnormalities in critical care patients, yet is limited in addressing the underlying complex injury. Human mesenchymal stromal cells (MSCs) metabolize and secrete anti-inflammatory and regenerative factors that can be of systemic benefit to acute, critical injury. When transplanted MSCs are limited in dose and rapidly cleared by the body, therefore prohibiting controlled exposure to cell therapy. We have developed a technology to maintain MSC viability and continuously deliver secreted factors into the blood stream in a clinical setting. MSCs were integrated into hollow-fiber bioreactor devices whereby the cells, separated by a permeable membrane, can directly and dynamically provide systemic therapy without entering the body. We present a human scale prototype of the technology that has shown sustained cell viability and function throughout manufacturing and report encouraging in vivo therapeutic trials in a canine model of ischemic acute kidney injury (AKI). We expect that a combined approach to optimize MSC therapy that employs pharmacology principles and cell delivery strategies will be essential to translating this stem cell product to humans for AKI and other critical organ dysfunction syndromes.

Abstract Number 74

Improvement of the 5L ACCUSOL CLEAR-FLEX Product Design for a Safe and User-friendly CRRT Therapy

Damien Valkeners[1], Jean-Pierre Hartman[1], Benoit Moreaux[1], Patrick Balteau[1]

[1]Baxter R&D Europe

Bicarbonate is a more physiological buffer for CRRT solutions. Due to the potential of calcium carbonate precipitation, these solutions are stored and sterilized in dual chamber bags. The ACCUSOL CLEAR-FLEX technology provides a 5 Liter container suitable for CRRT solution by using a peel-sealing technology. This container has two compartments to hold respectively a pH 9.0 concentrate of bicarbonate solution and a pH 2.0 electrolyte concentrate solution. The dual chamber bags have a seal between these two solution chambers, which must be broken to mix the solutions prior to use. If the user fails to break the seal between the chambers it is possible that only one chamber is infused into the patient (e.g. infusion of the bicarbonate solution alone), which can lead potentially to severe patient side effects. This misinfusion is a known issue for all CRRT solutions manufactured in multi-chamber bags. The 5L ACCUSOL CLEAR-FLEX product has been available for several years and occasional misinfusion events have been reported when the care provider connected the bag to the CRRT administration set without breaking the peel-seal. This abstract reports on product design improvements undertaken in the 5L ACCUSOL CLEAR-FLEX product to help prevent misinfusion.
The ACCUSOL CLEAR-FLEX film properties allow cohesive and/or adhesive seals according the temperature of the sealing dies. The improved bag design uses two adhesive (peelable) seals. To the first long peel-seal dividing the bag in two chambers to separate the active ingredients of the concentrate solutions, a second short peel-seal isolating the access system from the solution has been added. The opening of the long peel-seal allows for instant mixing of the concentrates to constitute the ACCUSOL solution. Only once the ACCUSOL solution is reconstituted, the opening of the short SafetyMoon seal allows infusion of the mixed solution into the patient. The sealing parameters, the shape and the width of the long and short peel-seals have been defined and validated in such way that the energy (force x displacement) needed to open the long peel-seal is always significantly lower than the energy needed to open the short peel-seal, ensuring the correct sequential opening of both seals.
The improvement of the ACCUSOL CLEAR-FLEX product through the introduction of the new short SafetyMoon seal will allow the additional safety needed to always make sure the right solution is delivered to the patient.

Abstract Number 75

The Effect of On-Line Hemodiafiltration On Dry Weight Adjustment In Intradialytic Hypotensive Prone Patients : Comparative Study Between Conventional Hemodialysis and On-Line Hemodiafiltration

Sun Woo Kang[1], Seok Ju Park[1], Tae Hee Kim[1], Yeong Hoon Kim[1]

[1]*Inje University, Busan, South Korea*

Introduction
Correct adjustment of dry weight after hemodialysis (HD) without any signs of hypervolemia is important. Intradialytic hypotension (IDH) is the most common complication during HD. The occurrence of IDH is 15-30 or even 50% of dialysis sessions. Intradialytic hypotension essentially augments mortality due to chronic overhydration and inability to reach proper dry weight. On-Line hemodiafiltration (olHDF) has been reported to reduce the frequency of IDH. The aim of this study is to assess the effect of olHDF on the hemodynamic stability and dry weight adjustment compared with low-flux HD.

Methods
IDH-prone HD patients at our center were enrolled. This study was designed as a cross-over trial with two phase (A arm : low-flux HD for 8weeks _ olHDF for 8weeks versus B arm : olHDF for 8weeks _ low-flux HD for 8weeks versus) and two treatment arms (olHDF versus low-flux HD), each phase lasting 8 weeks. We measured the proportion of water in the body with a body composition monitor (BCM).

Results
Twenty patients were enrolled, and nineteen patients completed the study. Not only the mean of interdialytic body weight gain but the frequency of IDH were not different between A arm and B arm (P=0.817, P=0.562). Consequently there were no significant differences in overhydrated amount during the two study phase, which was measured by BCM (A arm : P=0.875, B arm : P=0.655, table 1).

Conclusion
Our study did not show that On-Line hemodialfiltration gave more benefit to reduce the accumulation of body water compared with conventional hemodialysis.

		HD	On-Line HDF	p-Value
Interdialytic body weight	A arm	2.52±0.6	2.57±0.7	0.754
gain (kg)	B arm	2.53±0.6	2.54±0.5	0.889
UF for each dialysis	A arm	2.85±0.6	2.93±0.6	0.53
session (L)	B arm	2.92±0.6	3.05±0.6	0.263
Frequency of IDH	A arm	44.6±17.0	38.6±17.4	0.272
	B arm	42.8±16.7	28.6±7.9	0.093
Absolute value of	A arm	0.9±0.5	0.9±0.6	0.875
overhydration (L)	B arm	1.4±1.5	1.3±1.4	0.655
Frequency of	A arm	2.3±2.9	3.0±3.2	0.107
hyper/hypovolemia	B arm	3.0±3.6	4.0±3.1	0.197

Abstract Number 76

Low 25-Hydroxyvitamin D Level at Continuous Renal Replacement Therapy Initiation Predicts In-Hospital Mortality

Kyung Don Yoo[1], Hajeong Lee[1], Seung seok Han[1], Jung nam An[1], Yon Su Kim[1], Dong ki Kim[1]

[1]*Seoul National University Hospital*

Background: The low 25-hydroxyvitamin D (25(OH)D) level has been known to be associated with the development and prognosis of acute kidney injury (AKI) in critically ill patients. However, the association between serum 25(OH)D level and outcome of AKI remains to be clarified in patients initiating continuous renal replacement therapy (CRRT).

Methods: This prospective observational cohort study included patients with severe AKI requiring CRRT, from Nov. 2011 to Nov. 2012. Patients with end-stage renal disease were excluded. Biochemical data including 25(OH)D were measured at the time of CRRT initiation. Patients with 25(OH)D level below the median were included in the Low group and those with 25(OH)D level above the median were included in the High group. The primary outcome was in-hospital mortality, and the secondary outcome was duration of ventilator support and RRT.

Results: A total of 131 patients were analyzed. The mean age was 66.3 years and male patients were 73 (55.7 %). The mean APACHE II score was 29.18 ± 8.07. The median of serum 25(OH)D level was 6.90 ng/ml , and the mean serum 25(OH)D level were 3.97 ± 1.56 ng/mL and 12.47 ± 5.48 ng/mL in the Low group and the High group, respectively. There was no significant difference in baseline clinical characteristics including causes of AKI, Charlson comorbidity index between the groups. There was no significant difference in ventilator free days and RRT free days between two groups. However, the mortality rate was significantly higher in the Low group than in the High group (86.6 vs. 71.9 %, p=0.038). In survival analysis, low 25(OH)D level was proved to be an independent risk factor for in-hospital mortality after adjustment for by age, sex, mean arterial pressure, APACHE II ,SOFA score, c-reactive protein, hemoglobin, BUN and serum albumin (Hazard Ratio 1.63, 95% confidence interval 1.08–2.45;P=0.018).

Conclusions: In this study, we demonstrated that critically ill patients with AKI requiring CRRT showed severe 25(OH)D deficiency. Moreover, low 25(OH)D levelat the time of CRRT initiation might be associated with higher in-hospital mortality.

Abstract Number 77

Effects of a Novel Adsorbent on Septic Rats: in Vitro and in Vivo Study

jicheng zhang[1], feihu zhou[1], zhiyong peng[1], William Federspiel[1], John A. Kellum[1]

[1]*Center for Critical Care Nephrology, CRISMA Center, Department of Critical Care Medicine, University of Pittsburgh*

Introduction:
Sepsis is characterized by increased expression of cytokines in the blood. Hemoadsorption, by removing cytokines from the circulation, may attenuate the dysfunctional inflammatory response and improve outcomes.
Hypothesis:
We hypothesized that CTR, a new sorbent, can remove cytokines and improve organ function.
Methods:
CTR sorbent beads were filled into apharesis columns of three sizes: small (0.5ml), medium (1.0ml) and large (2.0ml). Each size column was tested using IL-6 capture in vitro. Next, rats were subjected to cecal ligation and puncture (CLP) and 18 hours later an extracorporeal circuit was established using the internal jugular and femoral veins. Animals were randomly assigned to receive treatment with either 0.5ml, 1ml, or 2.0ml columns (CTR0.5, CTR1 and CTR2 respectively) or sham treatment (n=10 each) for four hours. Blood was drawn at 18 hour (hr) after CLP, after the 4 hr treatment, and then at 48 hr and 72 hr after CLP. Plasma cytokines (TNF, IL-1_, IL-6, and IL-10), high mobility group box1 (HMGB-1), alanine aminotransferase (ALT) and serum creatinine were measured. Survival time was recorded.
Results:
In vitro IL-6 removal was accelerated with increasing bead mass. In vivo, survival rates to 7 days after CLP were 50%, 63.64%,

62.5%, 72.72% for the sham, CTR0.5, CTR1, CTR2. The baseline values (18_hr after CLP) of cytokines (TNF, IL-1_, IL-6, and IL-10), and the concentrations immediately after treatment remained constant and were not different among groups. At later time points (48 hr and 72 hr) after intervention, the cytokine concentrations were significantly lower in the CTR0.5 and CTR2 beads ($p<0.05$) treatment groups. There were no significant differences before treatments on HMGB-1, but after two days, CTR2 groups showed a significant decrease ($p<0.05$). There were no statistically significant differences reached on ALT and creatinine, but the results show strong evidence for late renal protection.
Conclusion:
CTR appeared to have a favorable effect on survival despite no immediate effects on cytokine removal. However, CTR did result in a late decrease in IL-6, IL-10, TNF and HMGB-1 (especially CTR2 beads). There were no significant effects on organ function, although there was a strong trend toward reducing kidney injury at 72 hrs.

Abstract Number 78

Effect of On-line Hemodiafiltration on Dry Weight Adjustment in Intradialytic Hypotension-prone Patients: Comparative Study of Conventional Hemodialysis and On-line Hemodiafiltration

Sunwoo Kang[1], Taehee Kim[1], Yeonghoon Kim[1]

[1]*Department of Nephrology, Inje University*

Introduction: Correct adjustment of dry weight after hemodialysis (HD) with no signs of hypervolemia is important. Intradialytic hypotension (IDH) is the most common complication during HD. IDH occurs in 15% to 30% and possibly in up to 50% of dialysis sessions. IDH augments mortality essentially due to chronic overhydration and the inability to reach the proper dry weight. On-line hemodiafiltration (ol-HDF) has been reported to reduce the frequency of IDH. The aim of this study was to assess the effect of ol-HDF on hemodynamic stability and dry weight adjustment compared with low-flux HD.
Methods: IDH-prone HD patients at our center were enrolled. This study was designed as a crossover trial with two phases (A arm: low-flux HD for 8 weeks followed by ol-HDF for 8 weeks vs. B arm: ol-HDF for 8 weeks followed by low-flux HD for 8 weeks) and two treatment arms (ol-HDF vs. low-flux HD), each phase lasting 8 weeks. We measured the proportion of body water using a body composition monitor (BCM).
Results: In a comparison of the systolic blood pressure (SBP) and diastolic blood pressure (DBP) reductions from the baseline blood pressure between the HD and ol-HDF groups, statistically significant differences were observed only in the SBP of the B arm (SBP: HD vs. HDF, 9.83 ± 6.64 vs. 4.62 ± 1.61 mmHg, $p = 0.036$; DBP: HD vs. HDF, 3.29 ± 4.05 vs. 1.86 ± 1.49 mmHg, $p = 0.261$). Neither the mean of the interdialytic body weight gains nor the frequency of IDH was different between the A and B arms ($p = 0.817$ and $p = 0.562$, respectively). In terms of dialysis modality, there were no significant differences in the amount of overhydration between the conventional HD and ol-HDF groups during the two study phases, as measured by the BCM (A arm: $p = 0.875$, B arm: $p = 0.655$).
Conclusion: Our study did not show that ol-HDF is more beneficial in reducing the accumulated body water in IDH-prone patients than conventional HD.

Abstract Number 79

Comparison of Drug Dosing Equations for Continuous Renal Replacement Therapy (CRRT)

Susan J Lewis[1], Anna Polso[1], John A Lee[1], Farzad Daneshvar[1], Abbie Leino[1], Bruce A Mueller[1]

[1]*University of Michigan, College of Pharmacy*

Background: No prospectively validated guidelines exist to provide drug dosing recommendations for patients receiving Continuous Renal Replacement Therapy(CRRT). Many different drug dosing equations have been published for this purpose, but the drug dosing recommendations derived from these approaches have never been directly compared.
Purpose: To quantify discrepancies between antibiotic dosing recommendations from 3 published dosing equations to each

other and to a commonly used CRRT drug dosing resource(Aronoff et al. 2007).
Methods: A 70 kg adult patient with Acute Kidney Injury, receiving CRRT was generated as the basis for this study. An effluent rate of 25ml/min(23.3 ml/kg/hr) was employed, based on the KDIGO CRRT effluent rate recommendations. Pharmacokinetic parameters for acyclovir, cefepime, daptomycin, fluconazole, gentamicin, levofloxacin, linezolid, meropenem, piperacillin, and vancomycin were obtained from the literature to calculate the adjusted doses from three different published CRRT drug dosing equations (Kroh [New Horizons 1995] , Reetze-Bonorden [Clin.Pharmacokinet 1993] and Bugge [Acta Anaesthesiol Scand 2001]). The calculated doses were standardized to mg/day to facilitate comparison. Clinically significant discrepancy between the calculated dose and the Aronoff dose was set at ≥ 30 % and the proportions of drug doses with clinically significant discrepancies from each equation were compared. Descriptive statistics were used to compare the calculated doses.
Results: Remarkable discrepancies between calculated doses with the three dosing equations were found. “Clinically significant discrepancies” from Aronoff were found in 70% of doses calculated with the Bugge equation, 60% with the Kroh equation, and 50% with the Reetze-Bonorden equation. These 3 equations had a tendency to yield lower doses compared with the Aronoff text, but discrepancy patterns were drug specific. The calculated doses(ranges) with Bugge, Kroh and Reetze-Bonorden equations accounted for averages of 75.4%(49-148%), 83%(22-160%), and 88.1%(17-135%) of the Aronoff doses, respectively.
Conclusion: This study unveils a wide variability among antibiotic dosing recommendations from published CRRT dosing equations which can potentially lead to inappropriate pharmacotherapy. Clinicians cannot trust that using published drug dosing equations will lead to consistently therapeutic antibiotic doses in patients treated with CRRT at the KDIGO recommended effluent rate.

Abstract Number 81

Effective combination therapy of Polymyxin-B direct hemoperfusion and recombinant thrombomodulin for septic shock accompanied by disseminated intravascular coagulation: a historical controlled trial

Masafumi Yamato[1], Yusuke Minematsu[2], Junya Fujii[2], Takumi Minato[2], Yoko Shima[1], Ryuta Fujimura[1], Naoko Morikage[1], Chisako Nakano[1], Akira Wada[1], Takahito Ito[1]

[1]Division of Nephrology, Osaka National Hospital, Osaka, Japan, [2]Division of Clinical Engineering, Osaka National Hospital, Osaka, Japan

Disseminated intravascular coagulation (DIC) and multiple organ failure often occur via the crosstalk between inflammation and coagulation, which is mediated by High Mobility Group Box 1 (HMGB1). In septic shock, Polymyxin-B direct hemoperfusion (PMX-DHP) ameliorates hemodynamics by endogenous cannabinoid adsorption and improves pulmonary oxygenation by indirect cytokine reduction through the adsorption of activated mononuclear cells. However, PMX-DHP has no direct effect on HMGB1 circulating in the plasma. In cases with DIC, recombinant thrombomodulin (rTM), an effective drug for DIC, exerts not only anticoagulation but also antiinflammatory properties via direct anti-HMGB1 activity. Therefore, a combination of PMX-DHP and rTM is expected to block the vicious cycle of a cytokine storm ending up with multiple organ failure in DIC. The aim of this study was to investigate the efficacy of the combination therapy for septic shock associated with DIC. This study comprised 22 consecutive sepsis-induced DIC patients who received PMX-DHP. The initial 8 patients were treated without rTM (historical control group), and the following 14 patients were given rTM (rTM group). The baseline Sequential Organ Failure Assessment (SOFA) score or age was not different between both groups. Sixty-day survival rate in the rTM group was significantly higher than that in the control group (85.7% vs. 37.5%, p=0.015). A combination of PMX-DHP and rTM may be effective in septic shock accompanied by DIC and expected to improve survival rates.

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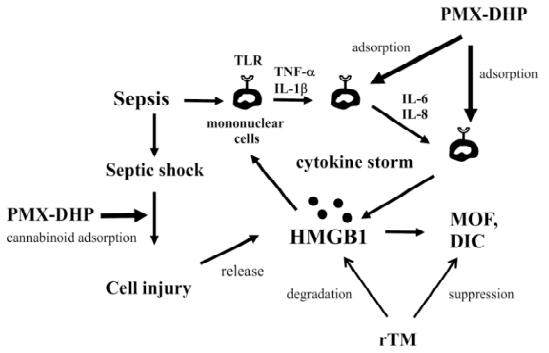
Figure
The putative mechanism of the combination of PMX-DHP and rTM for septic shock accompanied by DIC



PMX-DHP, Polymyxin-B direct hemoperfusion; rTM, recombinant thrombomodulin; HMGB1, High Mobility Group Box 1; TLR, toll-like receptor; MOF, multiple organ failure; DIC, disseminated intravascular coagulation.

Abstract Number 83

Timing of Renal Replacement Therapy and Mortality in Critically Ill Patients

Raghavan Murugan[1], Florentina E Sileanu[1], Gilles Clermont[1], Nicole M Lucko[1], John A Kellum[1]

[1]*University of Pittsburgh*

Raghavan Murugan, Florentina E. Sileanu, Gilles Clermont, Nicole Lucko, and John A. Kellum

Center for Critical Care Nephrology, CRISMA Center, Department of Critical Care Medicine, University of Pittsburgh, PA, USA

Purpose: Critically ill patients with acute kidney injury (AKI) requiring renal replacement therapy (RRT) are at a high risk of death. Whether earlier initiation of RRT is associated with lower mortality is uncertain. Among critically ill patients receiving RRT, we examined the association between timing of initiation of RRT on hospital mortality.

Methods: We performed an analysis of a large intensive care unit (ICU) dataset involving adults admitted to one of eight ICUs in a tertiary care academic medical center over 8-year period. We examined the risk and severity of AKI using KDIGO criteria. In order to account for indication bias, we matched patients with early RRT with those who never received RRT and those who

received late RRT using the Mahalanobis matching algorithm on the following variables: propensity for early RRT, baseline serum creatinine, rate of change in serum creatinine, volume of fluids infused in the first 24 hours of ICU admission, FiO2, serum potassium, and arterial pH.

Results: Of the 22,953 patients with AKI, 5,282 (23%) patients developed stage III AKI. After excluding patients who received RRT prior to ICU admission, or developed AKI prior to initiation of RRT or that were never on RRT and did not have an increase in serum creatinine within 2 days from reaching AKI stage III (n = 2,024), we assembled an analysis cohort of 3,258patients. Of patients with stage III AKI, 35.4% (n=1152) received RRT. Median time to RRT initiation after stage III AKI was 3 days. We defined early RRT as those receiving RRT ≤ 3 days and late RRT was defined as those receiving RRT after 3 days. We matched 575 patients with early RRT to 108 patients with late RRT. Baseline characteristics were similar after matching. Median length of ICU stay was longer for late RRT patients: early vs. late RRT, 12 (IQR, 6-24) vs.18 (IQR, 10-31) days, P <0.001. However, hospital mortality rate was similar (57.6% vs. 66.1%, P= 0.52).

Conclusion: Among critically ill patients receiving RRT, we found no difference in early vs. late initiation of RRT on hospital mortality. The increased length of stay in patients with late RRT could be due to immortal time bias.

Abstract Number 84

Poor Outcomes With RVAD plus CRRT

PRAMOD K GURU[1], Charat Thongprayoon[1], GINA M IACOVELLA[1], JOSHUA S BOTDORF[1], ANDREA S BRAUN[1], KIANOUSH B KASHANI[1], JOHN J DILLON[1]

[1]*MAYO CLINIC,ROCHESTER,MN,USA*

Purpose of the Study: Left and right ventricular assist devices (LVAD and RVAD) have been increasingly utilized in patients with severe myocardial dysfunction as either a bridge to heart transplant or as destination therapy. Despite improved survival over the years from refinement in both surgical techniques and the VAD device itself, the incidence of acute kidney injury (AKI) and need for continuous renal replacement therapy (CRRT) remains high. AKI is reported in around 21% of patients with LVAD, and is an independent predictor of mortality in these patients. Overall there is very limited data regarding outcomes for patients treated with both RVAD and CRRT. We reported our center's experience with patients receiving both modalities.
Methods used: Single center retrospective IRB-approved study of post cardiac surgery patients with RVAD who received CRRT for AKI between Jan 2007 and Dec 2012. Excluded patients were those who required only LVAD, extracorporeal membrane oxygenation (ECMO) or intra-aortic balloon pumps (IABP). We evaluated the patient characteristics, duration of mechanical support and survival.
Summary of results: Thirteen patients received combined CRRT and RVAD in the post cardiac surgery period. The types of surgery were coronary artery bypass surgery alone (N=2) or combined with valve surgery (N=4), valvular surgery alone (N=5), and other cardiac surgery (N=2). Surgery was emergent in 5 (38%) patients, and 5 (38%) patients required concurrent LVAD and/or IABP. The median age was 52 years, and 7 (54%) were male. The median preoperative serum creatinine was 1.4 mg/dl (IQR 1-2.1). Preprocedure congestive heart failure was present in 12 (92.3%) patients, diabetes in 5 (38.4%) and prior myocardial revascularization in 3 (23.1%).The median cardiopulmonary bypass time was 187 min (IQR 132-282). Post-operatively, 12 (92.3%) patients required vasopressor for hemodynamic support and 13 (100%) required mechanical ventilation. Mortality was 100% in those who received RVAD and required CRRT. The median survival of the cohort was eight days.
Conclusion: This small cohort of patients demonstrates a high mortality when CRRT is needed following RVAD implantation. This may relate to the poor prognosis of patients with severe right heart failure, the culprits of removing volume in these patients or the added mortality conferred by AKI. Further interventional studies to improve patient outcome in this patient population is warranted

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Abstract Number 85

In Vitro Clearance of Antiepileptic Medications via Continuous Venovenous Hemofiltration

Anagha Malur[1], Jacqueline Keesee[1], Danielle Jaskulski[2], Veena Nandwani[2], Paul McCarthy[2]

[1]East Carolina University, [2]University of Maryland

Introduction

Neuroscience Intensive Care Units are increasing in number and are caring for a wider array of neurologically related critical illnesses with multi-organ dysfunction. As a result the need for Continuous Renal Replacement Therapy (CRRT) is increasing in this setting. Since many of these patients require antiepileptic medications, an understanding of how CRRT may affect these medications is important.

We tested three common antiepileptic medications in an in vitro continuous venovenous hemofiltration (CVVH) model to examine how the therapy affects the medications. The sieving coefficients, filter absorption, and clearance of these medications were determined in this experiment.

Methods

Medication loss was quantified using an in vitro model of CVVH. Doses of valproic acid, phenytoin, and levetiracetam were injected into a bovine blood bath containing 3.8% citrate for the experiment. The NxStage machine and NxStage system one were used. The filter used in the experiment was the Polyethersulfone CAR 500. Blood flow was set at 200 mL/min, replacement was 0.9 normal saline pre-filter at 2L/hr. and ultrafiltrate was run at 1L/hr. The set-up was run for thirty minutes and samples were taken pre-filter, post-filter and from the ultrafiltrate for drug analysis. Medication levels were measured at an outside laboratory.

Results

Valproic acid had a calculated sieving coefficient of 17 percent and a filter absorption of 14 percent. The sieving coefficient of phenytoin was 27 percent and filter absorption was calculated to be 4 percent. Levetiracetam had a sieving coefficient 14 percent and a filter absorption of 4 percent.

Conclusions

All three antiepileptic medications had sieving coefficients of less than thirty percent, which is in a range similar to reports using other CRRT filters. The sieving coefficient was highest for phenytoin while valproic acid had the highest filter absorption. This in vitro study suggests that due to clearance and absorption, in clinical practice antiepileptic levels should be followed closely when CVVH is performed with the NxStage machine.

Abstract Number 86

Using Lean Thinking to Reduce Waste in Continuous Renal Replacement Therapy in a Large Academic Medical Center

C Brett Benfield[1], Michael Heung[1], Phil Brummond[1], Andrew Lucarotti[1], Maria Villarreal[1], Adam Goodwin[1], Rob Winnacott[1], Cheryl Talley[1]

[1]University of Michigan Health System

Purpose
Continuous Renal Replacement Therapy (CRRT) is a complicated therapy that requires efficient coordination between multiple departments. As part of a quality improvement initiative, we recently identified opportunities in our program related to standardization of processes and reduction of waste, particularly in distribution of CRRT solutions. The goal of this project was to use Lean thinking to improve programmatic efficiency.

Methods
An interdisciplinary team developed a Value Stream Map to identify the areas of waste associated with the current CRRT process. An A3 was created to aide in devising strategies for improving the process and these were prioritized by feasibility, sustainability, and expected impact. The primary intervention was a conversion of CRRT solution dispensing from an on-demand approach (requiring bedside nurse activation) to a just-in-time approach (requiring monitoring by pharmacy and delivery based on expected use). CRRT solution use was measured at baseline and in the post-intervention period. Adverse events related to CRRT were reviewed for relevance to process change in the post-intervention period. Surveys were administered to assess nursing and pharmacy staff satisfaction pre- and post-intervention.

Results
During the 11-month baseline period, there were 1554 CRRT patient-days, compared to 914 patient-days in the 6 months post-intervention period. There was no significant difference in prescribed CRRT solution flow rates between the periods (2381mL/hr vs. 2452 mL/hr, p=0.707). There was a significant reduction in CRRT solution bags dispensed per patient day in the post-intervention period compared to baseline (13.7 bags per patient day vs. 14.4 bags per patient day, p<0.001). No serious adverse events related to the process change were observed. Survey results revealed a significant improvement in satisfaction with the new process compared to baseline, and this was observed among both pharmacy and nursing staff. Based on institutional CRRT volume, the reduction in solution waste resulted in an estimated annual cost savings exceeding $50,000.

Conclusions
Utilizing Lean thinking, the team identified areas for improvement in delivery of CRRT. By streamlining the process based on the stakeholder needs of this institution, a significant decrease in CRRT solution waste was observed. This reduction in waste was also associated with an increase in staff satisfaction and significant institutional cost savings.

NURSING ISSUES

Abstract Number 87

Focus Directed Re-Education

Linda Topper[1], Alejandra Briseno[1]

[1]*Children's Hospital Los Angeles*

Purpose: At Children’s Hospital Los Angles, patients requiring Continuous Renal Replacement Therapy (CRRT) suffer from a multitude of diagnoses: AKI, sepsis, infants with metabolic defects, ingestions, acute hepatic encephalopathy, fluid overload, and VOD. PICU RN’s manage CRRT inter-operatively during liver transplant surgeries. The Pediatric Intensive Care Unit has seen a 17% increase in CRRT runs from 2009-2012 while the number of CRRT trained nurses has increased 16%. The RN sets-up, manages and troubleshoots the Prisma machine as well as provides patient care. The CHLA PICU RN CRRT requirement consisted of one 8 hour class and 2 days of bedside orientation with an experienced CRRT RN. An added complexity to ensuring CRRT RN competency was the wide variability of staff schedules, causing some CRRT RNs to have frequent CRRT encounters while others may only encounter CRRT yearly. The increasing complexity of patient diagnoses, the management differences related to these diagnoses, and the varied staff work schedules created a challenge to ensure CRRT RN competency. These challenges necessitated the development of a tool to meet the demands of CRRT competency.
Methods: In March 2012 an initial 50 question competency was developed to evaluate knowledge of CRRT and to ensure consistency of care. The competency was given to all CRRT RNs and to those taking the class for the first time. Based on questions with the highest percentage of incorrect answers it was determined that “focus directed re-education” was needed. This was accomplished by refining the PICU CRRT ORDER GUIDELINES to include expanded descriptions of the entire CRRT process. A revision was given to the next CRRT class in October 2012. In February 2013 mandatory biannual updates were initiated to keep all Hemofiltration Nurses updated on the most current practices.
Results: Since implementing the CRRT competency and biannual updates there has been a noticeable improvement in CRRT delivery as evidenced by increased accuracy and consistency in CRRT bedside management and a decrease in the percentage of incorrect answers on the CRRT competency from the February and June 2013 cohorts.

Conclusion: The initial CRRT competency for newly trained nurses has been decreased to 40 questions. We expect to see continued improvement in CRRT bedside management as “focus directed re-education” continues to be utilized during CRRT 2 day orientation and biannual updates.

Abstract Number 88

Implementing CRRT on a Neurocritical Care Unit

Danielle M Jaskulski[1], Brigid Blaber RN, MS[1], Paul McCarthy MD[1], Patricia Woltz RN, MS[1]

[1]*University of Marylnd Medical Center*

Background/Problem

Continuous renal replacement therapy (CRRT) is better tolerated by patients with acute neurological injury than other renal replacement modalities because hemodynamic changes and fluid shifts are minimized. However, because CRRT is high risk and low volume in the neurocritical population, those requiring CRRT care at our academic medical center were being transferred to other ICUs for care. In July 2012, Neurocritical Care leadership began planning for implementation of a CRRT program to better meet patient needs.

Methods/Interventions

An interdisciplinary team of staff nurses, educators, nurse practitioners (NPs), and physicians was formed and a multifaceted approach to educate staff nurses and NPs about CRRT care was developed. Nurses first completed an existing 8-hour CRRT core competency class provided by the hospital Professional Development department. Then, a 4-hour simulation-based skills lab was offered, taught in part by a CRRT industry representative. Nurse preceptors on other ICUs also provided CRRT learning experiences for neurocritical staff. On-line training modules were developed to make competency review accessible. When the team determined that 40% of the core nursing staff was CRRT care competent, the program went live with 24x7 on-call expert support from other ICUs. February 2013, the first patient requiring CRRT was treated on the Neurocritical Care unit, which currently averages one patient undergoing CRRT per month (range 0 – 2/month).

Results/Next Steps

Following establishment of the CRRT program on the Neurocritical Care unit, focus is shifting to patient-centric best practices and high quality CRRT care. Although competent, nurses continue to express feeling uncomfortable with CRRT. Unit specific written guidelines have been started that provide guidance around appropriate patient parameters and medical orders, initiation, down time, anticoagulation, trouble shooting, and expanded indications for the neurocritical patient population. A newly developed database captures important information for a unit-based interdisciplinary CRRT taskforce, which was recently established to regularly review cases, monitor patient outcomes, initiate quality improvement projects, and help identify potential research opportunities.

Abstract Number 89

Providing Optimal Tx Continuity through a Comprehensive Continuous Renal Replacement Therapy Nursing Education Program

Cynthia H McMillan[1], Ruth Morgan[1], Nichole Henley[1]

[1]*University of Virginia*

Purpose: To develop an education plan to optimize nursing competencies for the patient on Continuous Renal Replacement Therapy (CRRT)

Methods: As a result of nursing and physician concerns, CRRT troubleshooting difficulties, and series of clotted CRRT cartridges, a multifaceted education plan was developed in an academic medical center Medical Intensive Care Unit. The plan was derived from nursing interviews, CRRT machine-run information and on-site evaluation of machine management. Educational components include didactic, classroom, and hands-on learning. Classroom instruction involves dialysis principals, machine familiarity and hands-on simulation. Classroom instruction was reinforced though the provision of a handout reference at the completion of the session. . Continued support, in the form of preceptors with CRRT experience was also integrated into process to maintaining staff expertise in working with and troubleshooting the CRRT machine.

Summary of Results: 6 annual classes are provided each year to the ICU staff with additional classes added if needed. Currently, 63 MICU RNs are competent to provide CRRT to their patient

Conclusion: The educational program was successful. Fewer concerns are identified. The CRRT system run times have improved. The clotting of cartridges decreased. Nursing confidence regarding troubleshooting and maintaining continuity of patient care increased. The multi-faceted education program with activities to support sustained acquisition of knowledge and skills improved outcomes.