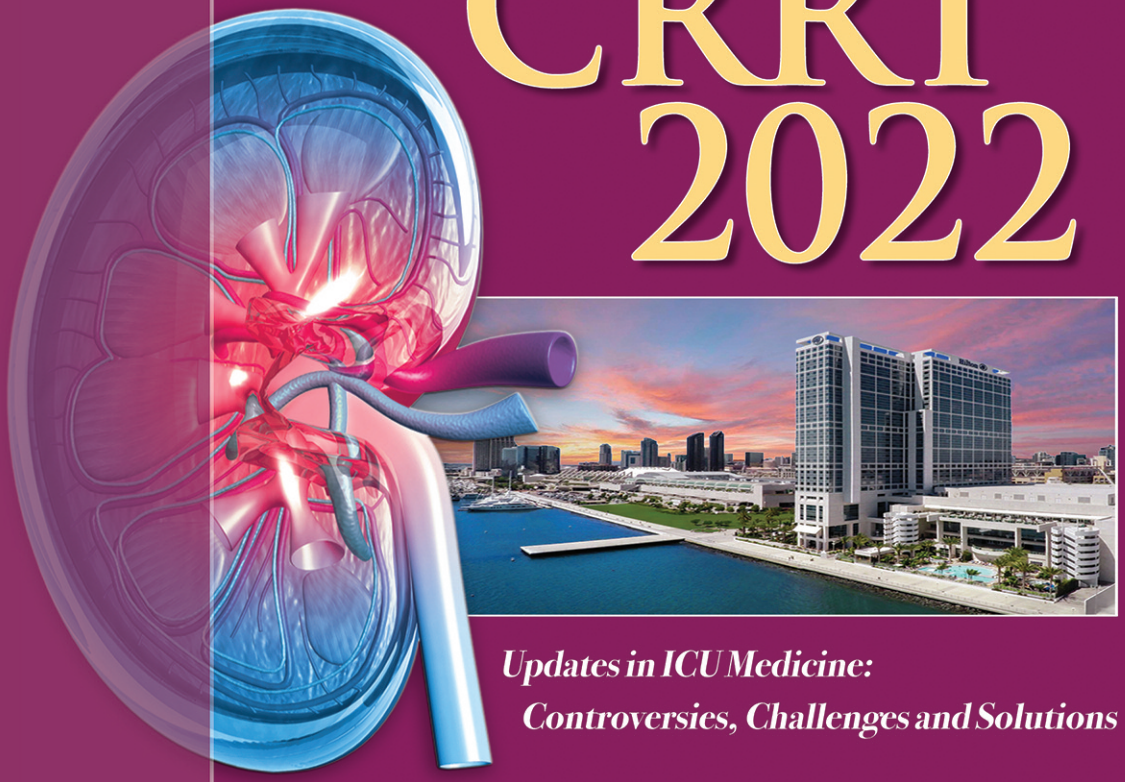
ABSTRACTS

THE 27TH INTERNATIONAL CONFERENCE ON
ADVANCES IN CRITICAL CARE NEPHROLOGY

AKI & CRRT 2022



Updates in ICU Medicine:
Controversies, Challenges and Solutions

MARCH 7-10, 2022

HILTON SAN DIEGO BAYFRONT
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Serum Sodium Trajectory During AKI and Mortality Risk.

Jonathan S. Chávez Iñiguez[1], Jorge I. Michel González [1], Pablo Maggiani Aguilera[1], Andrés E. De la Torre Quiroga[1], Andrea Luna Ramos[1], Guillermo Navarro Blackaller[1], Alexia Romero Muñoz[1], Ana T. Martínez Navarro [1], Ramón Medina González [1], Guillermo García García [1]

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Introduction.
Kidney plays a primary role in electrolyte homeostasis. The association between serum sodium level and mortality or the need for kidney replacement therapy during acute kidney injury has not been adequately explored.
Methods.
In this prospective cohort study, we enrolled patients admitted to the Civil Hospital of Guadalajara from August 2017 to March 2020. We divided patients into five groups based on the serum sodium level trajectories up to ten days following hospitalization, 1) stable normonatremia (serum sodium 135 and 145 mEq/L), 2) fluctuating serum sodium levels (increased/decreased in and out of normonatremia), 3) uncorrected hyponatremia, 4) corrected hyponatremia, and 5) uncorrected hypernatremia. We assessed the association of serum sodium trajectories with mortality and the need for kidney replacement therapy (secondary objective).
Results.
A total of 288 patients were included. The mean age was 55±18 years, and 175 (60.7%) were male. Acute kidney injury stage 3 was present in 145 (51%). Kidney replacement therapy started in 72 (25%) patients, and 45 (15.6%) died. After adjusting for confounders, 10-day hospital mortality was significantly higher in group 5 (HR, 3.12; 95% CI, 1.05 to 9.24, p = 0.03), and kidney replacement therapy initiation was higher in group 3 (HR, 2.44; 95% CI, 1.04 to 5.70, p = 0.03) compared with group 1.
Conclution.
In our prospective cohort, most patients with acute kidney injury had alterations in serum sodium. Uncorrected hypernatremia was associated with death, and uncorrected hyponatremia was correlated with the need for kidney replacement therapy.

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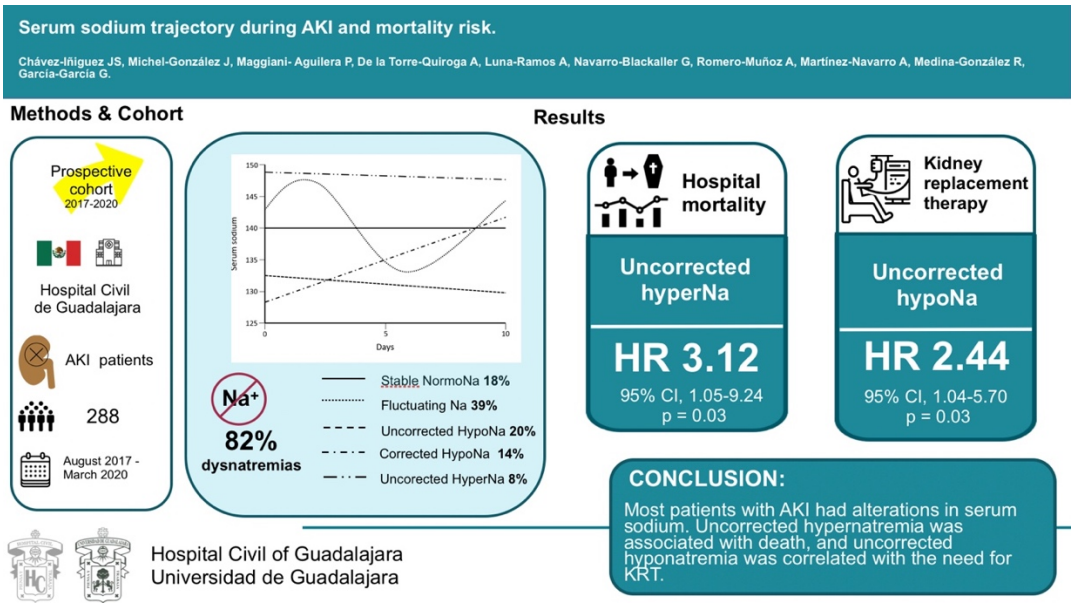

Abstract Category: A) Epidemiology and Outcomes from AKI

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Acute Kidney Injury (AKI) Subphenotypes and Acute Kidney Disease (AKD) in Patients with Severe and Critical COVID-19.

Jordan Tenzi[1], Maria Jose Dechia[1], Javier Hurtado[1]

Purpose of the study: Renal involvement, particularly AKI, has been frequently reported in critically ill patients during the COVID-19 pandemic. AKI associated with COVID-19 has adverse prognostic implications in terms of morbidity and mortality. The objectives of this study, in the context of severe and critical COVID-19, were (1) to determine the incidence of AKI, with their different subphenotypes, and AKD associated with COVID-19, (2) to determine the association of indirect factors with AKI (3) to determine the prognostic implications of renal involvement on morbidity and mortality and different degrees of organ support.
Methods: This was a prospective, observational and analytical study of a cohort of patients with severe and critical COVID-19 admitted to the ICU of Hospital Español. Descriptive and analytical analyses were performed; level for statistical significance: $p < 0.05$.
Results: The data for a total of 233 patients with severe and critical COVID-19 admitted to the ICU at Hospital Español between September 2020 and May 2021 were analyzed.
AKI associated with COVID-19 occurred in 47.9% (107/233) of the population studied, severe AKI associated with COVID-19 (KDIGO stages 2 and 3) occurred in 79.4% (85/107), and nosocomial AKI occurred in 47.7% (52/107).
AKD was found in 41.1% of those with AKI (44/107), with 29.9% (32/107) requiring kidney replacement therapy (KRT).
ICU mortality in patients with AKI was 72.9% (78/107), and those without AKI ICU mortality was 48.4% (61/126) ($p = .000$).
The multivariate analysis indicated normal renal function at discharge as a predictive factor of risk of death at discharge from ICU (OR .055, 95% CI: .014 - .213, $p = .000$).
Mortality based on the degree of organ support was as follows: invasive mechanical ventilation (IMV), 12/31 (38.7%); IMV + vasopressors, 86/109 (78.9%); and IMV + vasopressors + KRT, 26/27 (96.3%) ($p = .000$).
Conclusions: The incidence of AKI and AKD associated with COVID-19 in the ICU was high, with a predominance of more severe disease, and significantly higher mortality. The normalization of renal function was a protective factor of the risk of death. The degree of multiorgan support was associated with a progressive increase in mortality.

Abstract Category: A) Epidemiology and Outcomes from AKI

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Risk Factors for the Development of Persistent Acute Kidney Injury in Critically ill Patients. A Retrospective Analysis

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Introduction: Acute kidney injury (AKI) is a frequent complication in critically ill patients. Failure to recover beyond 72h (persistent AKI) is associated with worse outcomes. This study aimed to describe the occurrence of persistent AKI in critically ill patients in a large healthcare system in the U.S., to define the association between persistent AKI and mortality, and to identify risk factors for persistent AKI.

Methods: We conducted a retrospective study using the High-Density Intensive Care (HiDenIC) database, which includes patients admitted to the ICU from October 2008 to December 2014. We defined severe AKI as KDIGO stage 2 or 3, transient AKI as AKI that recovers within the first 72h, and persistent AKI as persistence at stage 3 for ≥72h. Primary and secondary outcomes were 90-day mortality and major adverse kidney events at 90 days (MAKE90), a composite of death, need for renal replacement therapy or persistence of AKI. Missing data were imputed. The prevalence of severe AKI, transient and persistent AKI was estimated using descriptive statistics. The association between persistent AKI and 90-day mortality was established and reported using multivariate logistic regression (MVL) and the Kaplan-Meier curve. The association between persistent AKI and MAKE90, and the identification of independent risk factors for persistent AKI, were established using MVL.

Results: We identified 119,783 critically ill patients out of a source population of 287,495. Of these, 38,107 (31.8%) developed severe AKI. Of patients with severe AKI, 36,424 (95.5%) had transient AKI, while 1,683 (4.4%) had persistent AKI, which accounts for 1.4% of the total population. Persistent AKI was associated with 90-day mortality (Fig.1). Persistent AKI was only second to a Charlson score ≥6 as the most important risk factor for 90-day mortality (OR 2.65, 95%CI 2.33-3.00), and was the most important risk factor for MAKE90 (OR 19.44, 95%CI 15.44-24.5). Baseline creatinine and Charlson score were the highest risk factors for persistent AKI.

Conclusions: Persistent AKI occurred in 1.4% of all critically ill patients, was associated with a 3-fold increase in 90-day mortality and a 20-fold increase in MAKE90. Our results suggest that the first 72h of AKI may be analogous to the ‘golden hour’, wherein interventions to prevent persistent AKI will decrease morbidity and mortality, particularly critically ill patients with worse baseline creatinine and multiple comorbidities.

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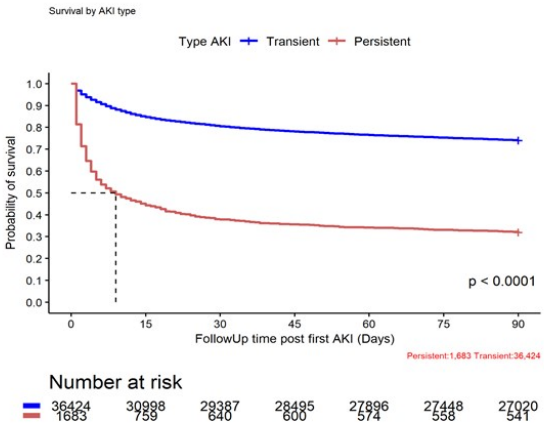

Abstract Category: A) Epidemiology and Outcomes from AKI

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Impact of acute kidney disease on the incidence of acute kidney injury in the intensive care unit

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Introduction
Acute kidney disease (AKD) is a kidney dysfunction sustained more than seven days and less than 90 days, and chronic kidney disease (CKD) is a kidney dysfunction sustained more than 90 days. From the previous studies, CKD was studied as a risk factor for acute kidney injury (AKI) in intensive care unit (ICU). However, the impact of AKD on the incidence of AKI was not fully studied.
Method
This is a single-center retrospective cohort study of critically ill patients admitted to ICU at the Pusan National University Hospital. We included adult (age ≥18 years) ICU admitted patients from January 2011 to December 2020. Patients without serum creatinine data before hospital admission and those having end-stage kidney disease were excluded. We divided patients into three groups based on the estimated glomerular filtration rate (eGFR) value between 1 year and 90 days before admission, and eGFR within 90 days of hospital admission; no kidney disease (NKD) as eGFR consistently higher than 60ml/min, AKD as eGFR ≥ 60ml/min between 1 year and 90days but decreased to <60 mL/min within 90 days of hospital admission, and CKD as eGFR consistently lower than 60ml/min. We defined AKI by KDIGO serum creatinine criteria. We compared the incidence of AKI in ICU by baseline kidney status.
Results
During the study period, 27,285 were admitted to ICU. A total of 4,066 were included in the study, excluding 679 patients who were younger than 18 years old, 22,463 patients without baseline creatinine, and 77 ESKD patients. The population was all Asian, median age of 67 (18-110) years, and 57.6% were male. At baseline, 2,690 (66.2%) had NKD, 405(10.0%) had AKD, and 971(23.8%) had CKD. In ICU, AKI was observed in 635(15.6%) out of 4066 patients. The incidence of AKI was the highest in AKD (17.2%, 70/405) followed by CKD (16.2%, 157/971) and NKD (15.2%, 408/2690). Among the 635 AKI patients, stage 3 AKI was more common in AKD (5.4%, 22/70) or CKD (5.3%, 51/157) compared to NKD (3.8%, 101/408).
Conclusion
We investigated the AKI incidence among patients admitted to ICU retrospectively. In summary, similar to CKD, AKI was more common and severe in AKD than NKD in patients admitted to ICU.

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Incidence And The Impact Of Acute Kidney Injury And Renal Replacement Therapy On Extracoporeal Membrane Oxygenation Patients

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Background: Acute kidney injury (AKI) is a well-known adverse event in patients supported with Extracorporeal Membrane Oxygenation (ECMO), and its impact on the outcome is highly controversial. The incidence of AKI in ECMO patients varies significantly due to the lack of consensual definition. The aim of this study is to identify the incidence of AKI in ECMO patients and its impacts on the outcome.

Methods: This was a retrospective cohort study in patients who underwent ECMO cannulation at Cho Ray Hospital between January 2019 and December 2019. We evaluated the incidence of KDIGO-defined AKI, continuous renal replacement therapy (CRRT) at pre-ECMO and post-ECMO support. We performed Cox proportional hazards model to test the association of CRRT and other factors with in-hospital mortality.

Results: There are 94 eligible patients of whom 69 (73.4%) survived. 33 (35.1%) patients had pre-ECMO AKI, 3 patitients have kidney function recovery post-ECMO and the incidence of post-ECMO AKI was 35.1% (33/94 patients). Amongst all AKI patients, 50 patients (79%) were classified as KDIGO-stage 3 AKI, and 46 patients (79%) required CRRT. KDIGO-stage 3 AKI, Pre-ECMO CRRT and Post-ECMO CRRT were factors associated with higher in-hospital mortality in univariate Cox regression model with hazard ratios (HR) of 13.98 (CI 95%: 1.87 – 104.05); 5.79 (1.91 – 17.56); 5.06 (1.42 – 18.03), respectively. The pre-ECMO CRRT (defined as CRRT prior to or within 24 hours of ECMO) remained an independent predictor for in-hospital mortality after adjusting for age, APACHE II score and initial serum lactate with HR 4.24 (CI 95%: 1.27 – 14.16) while post-ECMO CRRT was not (HR 3.08; CI 95% 0.82 – 11.54)

Conclusions: The incidence of ECMO-associated AKI was 49.1%. In our study, only the AKI requiring CRRT prior to ECMO was associated with in-hospital mortality while CRRT after ECMO insertion was not.

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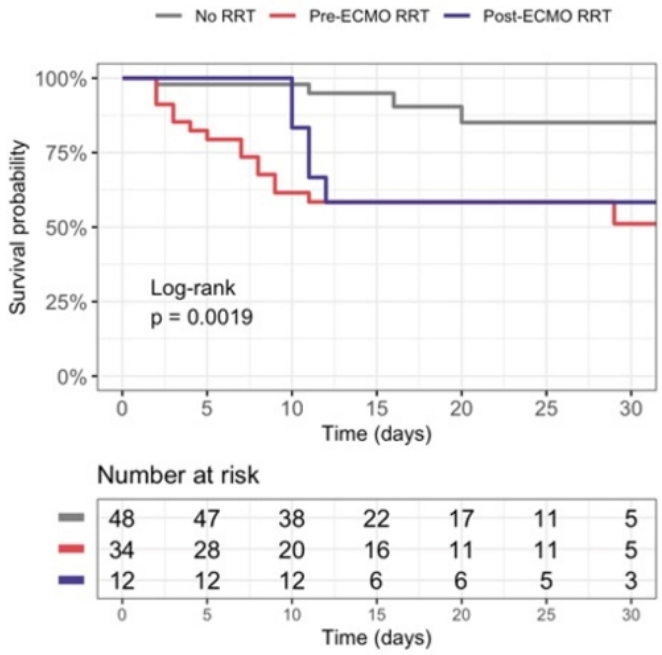

Abstract Category: A) Epidemiology and Outcomes from AKI

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Effect of AKI Stage on Clinical Outcomes and Residual Renal Function in Adult Patients Undergoing On-Pump Cardiac Surgery

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Cardiac surgery is performed for indications that are not primarily kidney-focused, but the resultant improvement in myocardial function may also lead to better kidney function. However, Cardiac Surgery Associated Acute Kidney Injury (CSA-AKI) may affect up to 30% of cardiac surgery patients and can lead to reduced renal function and other adverse clinical outcomes. We hypothesized that in patients with impaired kidney function at baseline, the severity of CSA-AKI would correlate with residual kidney function and clinical outcomes.

This retrospective study used electronic medical records from the Cerner® Real-World Data database of adult U.S. patients with baseline estimated glomerular filtration rate (eGFR) between 25-75 ml/min who underwent on-pump open valve or combined coronary artery bypass graft surgery during a 5-year period. Outcomes included incidence and stage of AKI (using Kidney Disease Improving Global Outcomes (KDIGO) via serum creatinine criteria) to post-operative Day 5 (POD5); eGFR between Day 6-90 and major adverse kidney events within 90 days (MAKE90) defined as: death, RRT, or ≥25% decline in eGFR relative to pre-surgery. eGFR values at baseline vs. within Day 90 in the same AKI group were compared using Wilcoxon-Mann-Whitney test.

Inclusion/exclusion criteria were met by 6,821 out of 22,045 open cardiac surgery patients. By POD5, 49.9% patients developed AKI (78.1% stage 1; 21.9% stage 2/3). Patients with AKI stage 2/3 experienced a decrease of ~7 mL/min in eGFR within 90 days ($p<0.001$) while the median baseline eGFR increased from 61.9 to 68.5 mL/min ($p<0.001$) in patients who did not develop AKI (Table). Incidence of MAKE90 in the overall cohort was 18.2%.

In this observational study of on-pump cardiac surgical patients with reduced baseline kidney function, we observed a decrease in eGFR from baseline to within 90 days in AKI stage 2/3 patients, while non-AKI patients exhibited improved eGFR in this timeframe. These data show a correlation between more severe AKI and sustained worsening of eGFR following cardiac surgery and point to eGFR as a robust clinical endpoint for AKI therapy trials.

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	No AKI	AKI Stages 1-3	AKI Stages 2/3
Baseline			
N	2,843	3,111	671
eGFR (mL/min), Median [25th, 75th]	61.9 [53.2, 69.0]	55.3 [44.5, 64.9]	54.3 [42.3, 64.9]
Day 90			
N	2,777	3,109	669
eGFR (mL/min), Median [25th, 75th]	68.5 [56.3, 81.5]	55.5 [41.0, 70.5]	46.7 [28.1, 65.3]
P value: eGFR baseline vs within Day 90	<0.001	0.007	<0.001
MAKE90, %	7.8%	28.7%	68.9%

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Acute Kidney Injury Is Associated With Increased In-Hospital Mortality And With Impairment Of Kidney, Lung, Motor and Immune Function 1 Year After Discharge for COVID-19

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Background: AKI is the most frequent complication after respiratory failure in COVID-19. AKI increases mortality risk, length of hospital stay and healthcare costs with possibile progression toward CKD. Study aims: 1) evaluation of AKI incidence in 1020 COVID-19 hospitalized patients; 2) comparison of AKI incidence in COVID-19 vs. pre-pandemic period; 3) establishment of out-patient follow-up for monitoring kidney, lung, motor and immune function; 4) creation of a biobank for biomarker discovery studies.
Methods: AKI incidence was calculated matching laboratory and administrative data of 26214 hospitalized patients in 2018-2019 and in 1020 COVID-19 patients in 2020-2021: KDIGO algorithms were applied for AKI grading. After 12 months from discharge, 232 COVID AKI patients and relative controls matched for age and gender were evaluated for kidney (eGFR, biomarkers of tubular damage NGAL, CCl-14, DKK-3), lung (DLCO, CT scan) and neuro-motor (SPPB, 2-min walking test, post-traumatic stress test-IES) function.
Results: Before pandemic, in-hospital AKI incidence was 18% (10% KDIGO 1, 5% KDIGO 2, 3% KDIGO 3): median age of AKI patients was 69. In-hospital mortality was 3.5 % in non-AKI group vs. 15% in AKI group in accordance with KDIGO stages. In COVID patients, AKI incidence increased to 37% (20% KDIGO 1,11% KDIGO 2, 6% KDIGO 3): median age of patients was 54. In-hospital mortality was 31 % in AKI group. After 12 months from hospital discharge, COVID AKI patients showed a persistent reduction of respiratory function (severe DLCO impairment <60%) related to the extent of CT scan abnormalities. AKI patients also presented motor function impairment and a worse post-traumatic stress response. GFR reduction was 1.8 ml/min in non AKI vs. 9.7 ml/min in AKI COVID patients not related to age. Urinary DKK-3 and CCL-14 were also higher in the AKI group. Last, IgG response after SARS-CoV-2 vaccination was significantly lower in AKI group.
Conclusion: AKI incidence was significantly increased during COVID-19 in respect to pre-pandemic period with an association with higher mortality in class 2-3 KDIGO. In the post-COVID follow-up, AKI was associated with lung and neuro-motor function impairment, a defective antibody response and a sudden GFR decline concomitant to the persistence of tubular injury biomarkers. These results suggest the importance of a nephrological and multidisciplinary follow-up of frail patients who developed AKI during hospitalization for COVID-19.

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Preliminary results of multicenter registry of critically ill patients with acute kidney injury and renal replacement therapy in Mexico: IRAM Registry

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Introduction: A reliable and objective source of information is required to measure the real magnitude that AKI and renal replacement therapy (RRT) represents in ICUs. To our knowledge, there are no registries in Mexico of AKI and RRT. The study aimed to present the preliminary results of the IRAM registry. The objectives of the IRAM registry are to estimate the prevalence of AKI with RRT requirements in Mexico ICUs and to describe which and how are the most prescribed modalities.

Methods: We performed a multicenter prospective registry of critically ill patients with AKI and RRT requirements from 14 ICUs in Mexico, all in teaching hospitals. Data were collected from each center in an electronic platform password-protected, designed expressly for the IRAM registry.

Results: Data from 179 patients collected from June 19th, 2021, to December 4th, 2021, were analyzed. COVID-19 was the predominant cause of ICU admission followed by septic shock (33.5 % and 32.4 %, respectively). Basal creatinine (Cr) was available for 83 % of the patients, mean baseline Cr was 1.65 ± 0.8 mg/dL. ATN was the main etiology (54%) for AKI. The predominant modality of RRT was IHD, present in 53 % (IHD + PIRRT) with CRRT as the second leading modality, in 46 %, only 1 patient required Peritoneal Dialysis (PD). At RRT initiation mean urine output of 0.66 ± 0.64 ml/kg/hr, fluid balance 5000 ± 338 ml, and fluid overload percentage of 6.9 ± 0.82 %. Cr at the initiation of RRT was 4.1 ± 0.23 mg/dL. About IHD prescription: mean treatment time was 203 minutes, 44.7% of the treatments were >240 minutes (PIRRT modality), QS 317 ml/min, QD 460 ml/min, and 78% of treatments had heparin anticoagulation. Prismaflex® was the preferred device to (98.5%), and the most common filter was Baxter ST150 ® (85.4%). The prescribed dose was 28.6 ± 8.5 ml/kg/hr, QS 153 ml/min, QD 1281 ml/h, 62% of treatments were without anticoagulation, 62% had heparin and 7% citrate Compared to IHD, CRRT achieved large ultrafiltration (2063 ml vs 1800 ml) with lower requirement for increased vasopressor during therapy (19 % vs 35 %). Finally, a total of 97 (54 %) died during the hospitalization.

Conclusions: In this preliminary analysis of the IRAM registry, we found that the most

prescribed modality in Mexican ICUs is IHD. The prescribed dose of CRRT is within the recommended goals. As expected, the UF achieved was higher with CRRT and whit a lower requirement of increased vasopressor during treatment.

Table 1. Characteristics of the study population

Characteristic	n=179
Age (years)	51 ± 18
Male, n (%)	109 (60.8)
Comorbidities, n (%)	
None	49 (27.3)
Diabetes mellitus	81 (45.2)
Hypertension	81 (45.2)
Chronic kidney disease	37 (20.6)
Heart disease	29 (21.7)
HIV	13 (7.26)
Rheumatologic disease	10 (5.5)
Others	20 (11.1)
Mains ICU admission	
COVID-19	60 (33.5)
Sepsis/Septic shock	58 (32.7)
Hemorrhagic shock	14 (7.4)
Surgery	13 (7.2)
Coronary artery disease	11 (6.1)
Trauma	6 (3.3)
Others	34 (18.9)
AKI etiology	Data from n=128
ATN	98 (76.5)
Pre-renal	22 (17.1)
Post-renal	1 (0.78)
Others	7 (5.4)
RRT initiation	
Urinary output, ml/min/kg	0.66 ± 0.64
Fluid balance, ml	5000 ± 338.45
Fluid overload, %	6.9 ± 0.82
Vasopressor use, % Overall IHD CRRT	 60.9 23 37
SOFA score, points	11 (0-18)
MAP, mmHg	80 ± 0.97
Creatinine, mg/dL	4.1± 0.23
BUN, mg/dL	91.83 ± 3.58
Potassium, mg/dL	5 ± 0.09
Phosphorus, mg/dL	6.96 ± 0.21
Arterial pH	7.28 ± 0.025
Bicarbonate, mg/dL	17.53 ± 0.49
Renal replacement therapy	Data from n=169
Peritoneal dialysis	1 (0.5)
Intermittent hemodialysis	90 (53.2)
CRRT	78 (46.1)
Achieved ultrafiltration	
Intermittent hemodialysis, ml	1800
CRRT, ml	2063
Increase in vasopressor	
Intermittent hemodialysis and PIRRT, %	37.5
CRRT, %	19

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Fluid Volume Overload is Associated with Poor Prognosis in Patients Hospitalized with Covid-19 and Acute Kidney Injury

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[1]*Hospital General Dr. Manuel González*

Purpose of the study: Acute kidney injury (AKI) has been associated with mechanical ventilation, renal replacement therapy (RRT) and mortality among patients hospitalized with Covid-19. Nevertheless, heterogenous outcomes among AKI stages in Covid-19 have been reported. The purpose of the present study is to evaluate the effect of fluid volume overload in AKI with progression of the disease and mortality among patients hospitalized with Covid-19.
Methods: Observational retrospective cohort study that included volume balances, clinical and biochemical data of 234 patients hospitalized with COVID-19 and AKI. Univariate and Cox regression analyses were used to evaluate the association of fluid overload with poor outcomes.
Results: The mean age of the patients was 57 ± 14 years, 69% were women, the mean body mass index (BMI) was 27.9±5.6 kg/m2, and median time in hospital were 11 (6-19) days. Overall, 47.3% had diabetes, 33.8% hypertension, less than 4% overt chronic kidney disease, and 47.9% had Community-Acquired AKI. The median global fluid overload was 434 (-1795 to +3449) cc [44.9% had global volume overload >+1000cc]. The rate of AKI 3, RRT, and mortality was 35.9%, 11.5% and 34.6%, respectively. Volume overload was associated with increased unadjusted risk for AKI 3, RRT, and mortality (HR= 4.104 [1.923-8.758]; HR= 5.461 [1.365-21.849]; HR= 4.279 [1.950-9.393], respectively; $p<0.05$ for all). After adjusting for demographics and comorbidities (Model 1) the risk for AKI 3, RRT, and mortality was HR= 5.793 (2.527-13.279), HR= 5.461 (1.365-21.849), and HR= 4.590 (2.062-10.219), respectively ($p<0.05$ for all). Likewise, when biochemical parameters were added to model 1 (model 2), those with volume overload reaming having greater risk for AKI 3, RRT, and mortality (HR= 5.941 [2.595-13.601]; HR= 5.610 [1.405-22.393]; HR= 4.472 [1.998-10.012], respectively; $p<0.05$ for all).
Conclusion: In the setting of AKI, fluid volume overload was associated with poor prognosis among hospitalized patients with Covid-19.

Table on following page

Variables	AKI 1 (n= 116)	AKI 2 (n= 34)	AKI 3 (n= 84)	p value
Age (years)	55.4 +- 14.5	54.7 +- 13.7	60.6 +- 12.7	0.017
Female sex (%)	70.7	76.5	64.3	0.384
Body Mass Index (kg/m2)	28.8 +- 5.9	29.8 +- 6.4	31.8 +- 6.9	0.269
Type 2 Diabetes (%)	40.4	57.1	53.6	0.123
Blood pressure >140/90 mmHg (%)	33.7	21.4	39.1	0.248
Chronic Kidney Disease (%)	0.0	3.6	8.7	0.010
Community-Acquired AKI (%)	65.5	52.9	21.4	<0.001
Days in Hospital (d)	8 (6-14)	16 (10-24)	16 (10-24)	0.480
Vasopressor use (%)	12.4	37.9	50.0	<0.001
Mechanical Ventilation (%)	21.9	48.3	70.8	<0.001
D dimer	0.49 (0.30-0.84)	0.54 (0.24-1.17)	0.90 (0.40-2.06)	0.002
Blood Urea Nitrogen (mg/dL)	19 (14-28)	26 (21-35)	31 (19-56)	<0.001
Lactic Dehydrogenase (IU/L)	354 (251-479)	393 (297-499)	417 (278-556)	0.155
C-Reactive Protein (mg/dL)	14.81 (6.47-21.60)	17.88 (7.40-21.20)	17.44 (11.80-27.90)	0.045
Ferritin (ng/mL)	533 (325-1016)	950 (447-1276)	800 (500-1457)	0.003
Serum Creatinine at admission (mg/dL)	1.03 (0.81-1.25)	1.11 (0.90-1.41)	1.23 (0.91-2.31)	0.001
Renal Replacement Therapy (%)	2.0	3.8	29.2	<0.001
Volume Overload >1000 (%)	37.9	33.3	59.5	0.057
Mortality (%)	17.2	20.6	64.3	<0.001

10

CENTER VARIATION IN LENGTH OF STAY FOR PATIENTS WITH HOSPITAL-ACQUIRED ACUTE KIDNEY INJURY IN ENGLAND

Javeria Peracha[1], David Pitcher[1], Shalini Santhakumaran[1], Retha Steenkamp[1], James Medcalf[2], Jamie Day[6], Dorothea Nitsch[3], Graham Lipkin[4], William McKane[5]

[1]*UK Renal Registry,* [2]*University Hospitals Leicester NHS Trust,* [3]*London School of Hygiene and Tropical Medicine,* [4]*University Hospitals Birmingham NHS Trust,* [5]*Sheffield University Hospitals NHS Trust,* [6]*Getting it right First Time*

Background and Aims:
Acute kidney injury(AKI) is associated with longer length of hospital stay(LOS) for affected patients; contributing to patient morbidity and healthcare costs. Implementation of AKI care quality improvement interventions have consistently been shown to reduce patient LOS however, suggesting its measurement may serve as a valuable AKI care quality indicator for hospitals.

In this study, we set out to explore, for the first time, unwarranted center variation in LOS for patients who develop hospital acquired AKI(HA-AKI) across England.

Method:
Analysis was undertaken using a routinely collected national database of patients with biochemical evidence of AKI, linked with NHS hospitals administrative data.

LOS was defined as the number of days between 1st AKI alert and discharge. A negative binomial model was used to generate predicted LOS for patients with HA-AKI at each hospital trust using age, sex, primary diagnosis, comorbidity score, AKI severity, admission method, month of AKI alert and critical care attendance.

Variation in "observed LOS – predicted LOS" values across centres were then compared using a funnel plot. Potential associations between centre LOS and readmission rates were also explored.

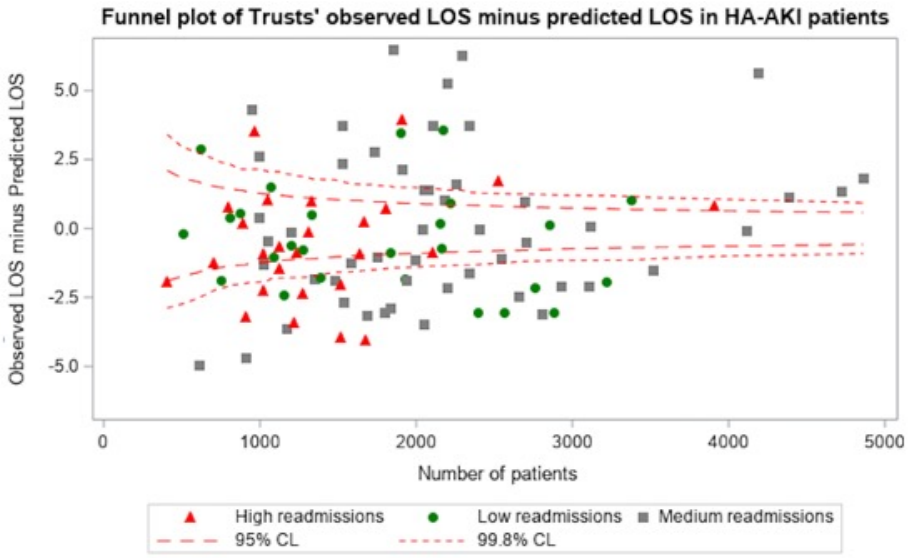
Results:
250,504 HA-AKI episodes were studied in total, across 103 NHS hospital trusts between 01/01/2017 – 31/12/2018.

Median LOS following HA-AKI alert for patients in our cohort was 8 days (IQR 3-17). Significant variation was noted in "observed - predicted LOS" values (Figure 1), with 55/103 trusts classed as outliers (99.8% control limits). When analysis was limited to patients with more severe AKI (stages 2 or 3) at presentation this number fell to 10/103 (99.8% control limits). Risk factors for longer LOS included male sex, advancing age, higher comorbidity score, more severe AKI at presentation, emergency admission and critical care attendance. Patients with hip fractures experienced the most variation in LOS nationally.

1in5 patients had an emergency readmission within 30days of discharge, with no association

observed between trusts “observed – predicted LOS” values and readmission rates(Figure 1).

Conclusion:
There was considerable centre-variation in LOS for patients with HA-AKI across England, despite adjustments for patient 'case-mix'. Further interrogation of patient and centre-level factors underlying this variation will likely help inform development of future AKI quality improvement interventions.



Negative Binomial Model adjusted for age, sex, AKI alert level, critical care attendance, comorbidity score, admission method, month of admission and diagnosis group, excluding patients who died in hospital

Confidence limits computed using empirical bootstrapping

HA-AKI = Hospital-acquired Acute Kidney Injury

LOS = Length of Stay following AKI alert

11

Impact of COVID-19 pandemic on trends in acute kidney injury (AKI) in England

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Background and Aims:
A high incidence of acute kidney injury(AKI) has been reported for patients with COVID-19 globally. During the "first wave" of the pandemic in England, concerns were raised regarding surging demand for acute renal replacement therapies and high mortality rates for patients with AKI, particularly across intensive care settings.

The aim of this study was to use national datasets to carry out a descriptive analysis of the impact of the pandemic on the epidemiology of AKI across England.

Method:
We identified patients with biochemical evidence of AKI using a routinely collated national dataset, linked to hospitals administrative data and national mortality feeds. We restricted our cohort to NHS Hospital Trusts with complete data available for time period 'January 2020 - July 2020'. Patients with COVID-19 were identified via data linkage from 'Public Health England' and included in our analysis if an AKI alert occurred following the date of a COVID positive test.

The total number of AKI alerts from included trusts were compared to the same time period in 2019. We also compared 30-day mortality rates (from the date of first AKI alert) using multivariable logistic regression modelling, stratifying results by sex, age group and month of AKI alert.

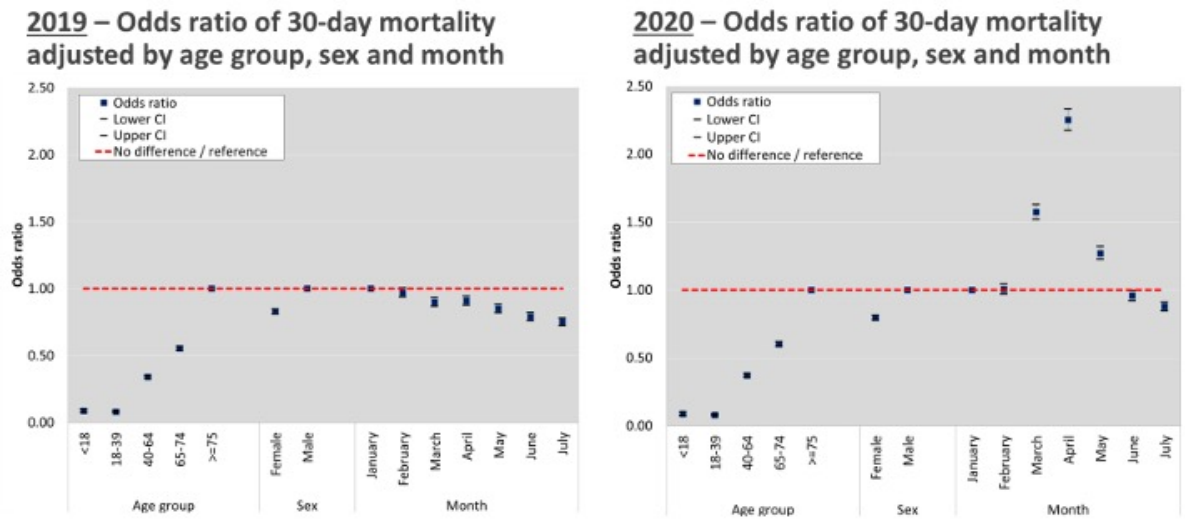
Results :
The total number of patients with AKI alerts January - July 2020 (N=231,818) was lower than the same time period 2019 (N=279,118). The odds ratios(OR) for death following an AKI alert in different sex and age categories were similar across both time periods. However, when comparing seasonal trends in mortality risk for patients with AKI, OR for mortality in Spring 2020 were significantly elevated compared to winter months, such that patients were twice as likely to die April 2020 vs January 2020 [OR 2.25, CI 2.17-2.33], a trend not observed in 2019 (Figure 1).

Patients with COVID-19 were on average 2.6 times more likely to die within 30days of an AKI alert than patients who did not have COVID.

Conclusion:
We found an overall reduction in incidence of AKI in England during the first wave of the COVID-19 pandemic (Spring 2020). This likely reflects dynamic changes to delivery of

healthcare services nationally e.g.accessibility of clinical services/blood tests and patient attitudes. Patients with COVID-19 who developed AKI were at an increased risk of death and further risk-adjusted analysis is now required, alongside assessment of longer-term patient outcomes.

Figure 1 Odds ratio by month for 30-day mortality after AKI alert for AKI patients in 2019 VS 2020, adjusting by age and sex



Abstract Category: A) Epidemiology and Outcomes from AKI

12

Center Variation In Seasonal Mortality Risk For Hospitalised Patients with Acute Kidney Injury In England

Javeria Peracha[1], Esther Wong[1], David Pitcher[1], Anna Casula[1], Retha Steenkamp[1], James Medcalf[3], Dorothea Nitsch[2]

[1]*UK Renal Registry,* [2]*London School of Hygiene and Tropical Medicine,* [3]*University Hospitals Leicester NHS Trust*

Background and Aims:
Incidence of Acute Kidney Injury (AKI) is known to be seasonal, peaking in winter months. Previous studies have suggested that seasonality of AKI is likely to be influenced by the seasonality of the underlying acute illnesses commonly associated with AKI and also suggest that mortality for patients with AKI may be higher in winter months. In this study we set to explore, for the first time, seasonal trends in AKI incidence and mortality for patients hospitalised across England and investigated whether these trends varied across different NHS hospital trusts.

Method:
We utilised a linked national database of patients with biochemically detected AKI and their hospitals administrative data. We identified hospitalised patients with biochemically defined AKI between January - December 2017 at 90 NHS Trusts. Seasonal odds ratios for mortality were generated using multivariable logistic regression, adjusting for season, primary diagnosis, comorbidity score, age, elective/emergency admission, peak AKI stage, ethnicity, socio-economic status, community/hospital acquired AKI and sex.

Results
130,434 AKI cases were studied in total. Incidence of AKI was 11% higher in winter (December-February) compared to summer (June-August). Patients with AKI in Winter were older, more co-morbid, more likely to have an emergency admission and AKI stage 3.

In the fully adjusted model, odds ratio for mortality in winter was still significantly higher (25%) than in summer [OR 1.26 (1.22-1.29), $p<0.01$]

When looking at seasonal mortality trends across all 90 hospital trusts, there was slightly more variation when comparing Autumn/ Winter to Summer vs Spring to Summer (Figure 1).

Conclusion:
There was an increased incidence of AKI across hospitals in England during winter months and also an increased risk of mortality, which persisted despite adjusting for a wide range of factors including patient diagnosis group. There was also more center-variation in mortality risk in colder months. This raises concerns about the possible impact of "winter-pressure" across the English NHS on outcomes for patients with AKI and merits further investigation.

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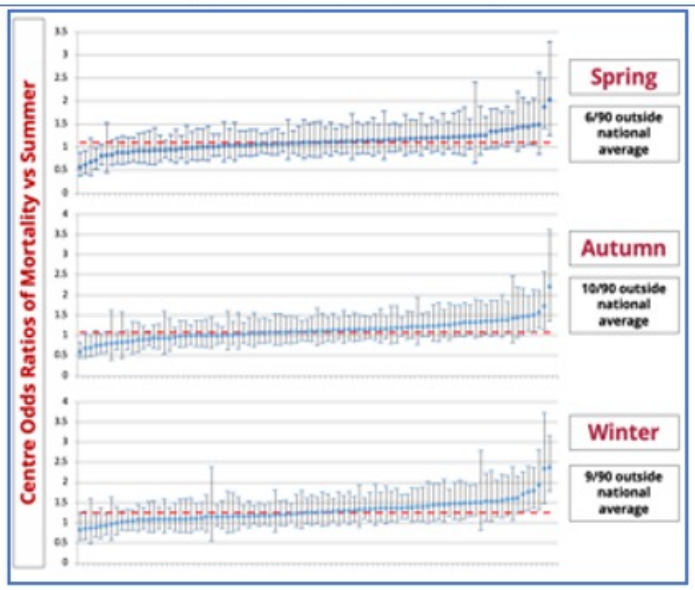
Figure 1 : Adjusted Odds ratio of mortality for patients hospitalised with AKI in each season (vs summer) by renal centre. Red line shows national average.



Abstract Category: A) Epidemiology and Outcomes from AKI

13

The Association of Erythropoietin Levels and Long-term Outcomes following Severe Acute Kidney Injury: A Post-hoc Analysis of Hormonal Status in Post-AKI Survivors (HAKI Study)

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Background: Acute kidney injury (AKI) survivors are at an increased risk of chronic kidney disease (CKD), end-stage renal disease, and mortality. Little is known about the effect of erythropoietin (EPO), major hormone producing by fibroblast-like cell in a kidney, in post-AKI setting. We aimed to investigate the role of EPO as a predictor of long-term outcomes in post-severe AKI survivors.

Methods: We performed a retrospective analysis of post-AKI cohort which was conducted between August 2018 to December 2021. Adults who survived from severe AKI stage 2-3 were enrolled into the study. The measurement of EPO level was obtained at the first visit of post-AKI clinic (1 month after hospital discharge). The primary outcome was the mortality at 12 months. The secondary outcomes included renal replacement therapy, persistent renal dysfunction, incidence of CKD, progression of CKD, the amount of albuminuria, and anemia status at 12 months.

Results: Eighty-two patients were enrolled into the study. Median EPO level was significant higher in non-survivors than survivors, 33.85 (16.2, 50.7) vs 12 (7.9, 21.7), p = 0.001. EPO level predicted mortality with an area under the receiver operating characteristic curve of 0.72. The multivariable analysis adjusted with severity of AKI, cause of AKI, co-morbidities, and baseline renal function demonstrated that high EPO level associated with higher mortality (p = 0.018). The best cut-off EPO level was 16.2 mU/mL. The high-level group had significantly higher mortality compared with low-level group (14.7% vs 2.1%, p = 0.042). The hematocrit level was significantly lower in high-level group compared with low-level group at 12 months (33.4±1.4% vs 36.5±1.0%, p = 0.038).

Conclusions: Plasma EPO appears to be a useful marker for predicting long term outcome in AKI patients who survived from severe AKI.

14

Acute Kidney Injury and Fluid Accumulation Following Neonatal Sepsis

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Background:
Acute kidney injury (AKI) and fluid accumulation (FA) are associated with increased morbidity and mortality in children and adults with sepsis. Sepsis is a common occurrence in the neonatal intensive care unit (NICU), yet data on neonatal AKI and fluid accumulation following sepsis are sparse. We aimed to describe the incidence of neonatal AKI and FA following sepsis.
Methods:
Retrospective chart review of NICU patients with a positive blood culture, admitted to Cincinnati Children's or University of Cincinnati between 6/2020-6/2021 was performed. Exclusion criteria: <5 days of antibiotics or no serum creatinine (SCr) data (unless secondary to mortality), or presence of a congenital kidney anomaly with dialysis dependence. The primary outcome was AKI, defined by the neonatal modified Kidney Diseases: Improving Global Outcomes SCr definition. Additional data collected: demographics, medications, and daily fluid balance. FA was calculated for 7 days after positive culture by: cumulative net fluid balance (L)/dry weight (kg). FA was not adjusted for insensible losses. Statistical analysis included Fisher's exact test, x^2, Mann-Whitney U test, and odds ratios. Baptista-Pike method was used to calculate 95% confidence intervals.
Results:
51 neonates had 54 sepsis episodes with a 33% (n=18) incidence of AKI. There was a 24% mortality rate (n=11), with 4 occurring prior to 48 hours. These 4 subjects were excluded from FA analysis secondary to incomplete data, and one was presumed to have AKI despite no SCr measurements. AKI stage ≥ 2 accounted for 53% (n=9). No subjects received renal replacement therapy. Subject demographics, nephrotoxic antibiotic exposure, and caffeine exposure did not differ between AKI and no AKI subgroups (table 1). Subjects with AKI were more likely to require vasopressor support (OR 4.5, 95%CI 1.2-15.1, p=0.040) and had more SCr measurements (7 [IQR: 4,8] vs. 3 [IQR: 2,6], p=0.013). Median peak FA to day 7 was 30% [IQR: 23%,47%] with median time to >10% FA being 2 days [IQR: 1, 3]. FA >10% in the first 24 hours was associated with AKI (57% vs. 15%, OR 7.3, 95% CI 1.5-40.7, p 0.005). Mortality risk was increased in subjects with any AKI (44% vs 12%, OR 5.6, 95%CI 1.13-32.5, p=0.024) and FA >10% in the first 24 hours (38% vs 6%, OR: 9.7, 95%CI 1.3-119.0, p=0.011).
Conclusion:
Neonates with sepsis who experience AKI are at increased risk for fluid accumulation in the first 48 hours as well as NICU mortality.

Table on following page

Variable	AKI (n=18)	No AKI (n=36)	p value
Male Sex	8 (44%)	19 (51%)	0.569
Race			>0.999
Black	7 (39%)	12 (35%)	
White	11 (61%)	22 (65%)	
Birth Gestational Age (weeks)	25 [IQR: 22,33]	28[IQR: 26,37]	0.0732
Corrected Gestational Age (weeks)	31 [IQR: 27,37]	36 [IQR: 27, 38]	0.5655
Small for Gestational Age	3 (17%)	6 (17%)	>0.999
Caffeine Exposure	9 (50%)	17 (47%)	>0.999
Vancomycin Exposure	10 (56%)	23 (66%)	0.555
Aminoglycoside Exposure	5 (55%)	5 (45%)	0.153
Vasopressor Exposure	10 (55%)	7 (20%)	0.013
Fluid Accumulation at <=24 hours	8 (57%)	5 (15%)	0.005
Mortality	7 (44%)	4 (12%)	0.024

15

Furosemide Responsiveness as a Predictor of Occurrence of Acute Kidney Injury (AKI), AKI Progression and Need for Kidney Replacement Therapy (KRT) among Critically-ill Hospitalized Patients: A Single

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Objective: This study aimed to determine the predictive factor of furosemide responsiveness (FR) in the occurrence of acute kidney injury (AKI), AKI progression and need for kidney replacement therapy (KRT) among patients admitted in the critical care units of St. Luke's Medical Center- Quezon City, Philippines from March 1, 2016 to February 28, 2021

Methods: This retrospective cohort included adult critically-ill patients given a single bolus of intravenous furosemide. We collected clinical and laboratory data, as well as urine output recorded hourly for the first 6 hours and cumulatively for 12 hours and 24 hours following furosemide administration. Patients were assessed for the occurrence of AKI or AKI progression, and for the need for KRT within 7 days after furosemide administration.

Results: We analyzed a total of 253 adult critically-ill patients—70 with no AKI and 183 with AKI at the time of furosemide administration. Receiver operating curve (ROC) analysis revealed that among patients with no AKI, FR was able to predict the occurrence of AKI and eventual need for KRT within 7 days with an area under the curve (AUC) values of 0.8. The best cutoff values identified were 33 mL/mg/4h for occurrence of AKI and 24 mL/mg/4h for eventual need for KRT. Furthermore, FR was able to predict AKI progression and eventual need for KRT within 7 days among critically-ill patients with AKI with AUC values of 0.76 and 0.77, respectively. The best cutoff values identified were 27 mL/mg/6h for AKI progression and 26.5 mL/mg/6h for eventual need for KRT. The predictive factor of FR was maintained when adjusted for several factors such as the presence and stage of CKD, heart failure, various nephrotoxic exposures, prior use of loop diuretic or other diuretics, need for pressor and/or inotrope, urine output in the prior 12 hours, creatinine clearance <20 mL/min and hypoalbuminemia.

Conclusion: Despite the use of varying doses of furosemide, FR has a good predictive ability in identifying critically-ill patients who are likely to have eventual occurrence of AKI, AKI progression, and/or need for KRT.

Abstract Category: B) Research in AKI

16

Nutritional intervention in intensive care unit patients undergoing continuous renal replacement therapy

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Nutritional intervention in intensive care unit patients undergoing continuous renal replacement therapy

Background
Providing adequate calories and protein constitutes an important part of critical care, and inadequate nutrition for critically ill patients is associated with poor prognosis. Therefore, increased loss of amino acids, electrolytes, and water-soluble vitamins during continuous renal replacement therapy (CRRT) could be a therapeutic target. We evaluated whether enforcing protein, trace elements and vitamin supply could improve the prognosis of CRRT patients.
Methods
Quality improvement study. A nutritional intervention (100 mg/day of Thiamine, 25–30 kcal/kg of energy, 1.8 g/kg of protein, and 50–100 mcg/day of microelement with selenium) was conducted in patients subject to CRRT with AKI from May 2020 to December 2020. The primary outcomes were 28-day mortality, CRRT day, ICU stay, and ventilator-free day, and the outcomes before and after the intervention were compared.
Result
Total 88 patients were included during the study period and compared with 173 patients in the previous year. The average age was 68 years old, both male predominant. There were 34 (13%) patients with ECMO, 212 (81.2%) patients using ventilator. There were 64 (24.5%) pneumonia with ARDS patient, 54 (20.7%) cardiac disease, 24 (9.2%) UTI sepsis, 33 (12.6%) gastrointestinal bleeding and sepsis, 22 (8.4%) cerebral hemorrhage, and others. The main reason for CRRT was hemodynamic instability. Baseline characteristics including APACHE-II score, SAPS 3, and SOFA were not significantly different between the nutritional intervention and the non-intervention patients. Nutritional intervention did not induce significant changes in 28-day mortality (44.5% versus 43.2%, $p = 0.19$) and CRRT days (8.1 ± 8.1 versus 6.2 ± 5.2, $p = 0.05$). However, nutritional intervention showed improvement in ICU stay (27.6 ± 26.3 versus 20.2 ± 21.4, $p = 0.02$) and ventilator-free days (49.1 ± 57 vs 40.7 ± 46.9, $p = 0.02$).
Conclusion
This study suggests that support for protein, trace elements, and vitamins may have a positive effect in CRRT patients. Therefore, the nutritional requirements of patients with CRRT should be carefully assessed, individualized, and considered as an important axis of CRRT treatment.

17

Biomarkers of Kidney stress During Early in Critical Illness Identify Patients with Impaired Kidney Function at ICU Discharge when Assessed using Cystatin-c but not Creatinine.

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Introduction:

During critical illness kidney injury is often sub-clinical but may lead to adverse kidney outcomes. The Nephrocheck™ assay is a combination two urinary biomarkers (TIMP-2.IGFBP-7) which identifies renal tubular stress and predicts risk of Acute Kidney Injury (AKI). We investigated the association between kidney stress during early critical illness and kidney function at ICU discharge.

Methods:

Participants were all inpatients at a tertiary critical care unit London, UK, half were major trauma admissions. TIMP-2.IGFBP-7 was measured on days 1,3,5, and 7. Patients who died in ICU were excluded. For each patient peak TIMP-2.IGFBP-7 within first 7 days of ICU admission was categorised as: Low risk (<0.3), Low-Medium Risk (0.3-0.99), High-Medium Risk (1-2) or High Risk (2+). Estimated Glomerular filtration rate (eGFR) at ICU discharge was assessed using Creatinine and Cystatin C. Differences in eGFR between groups based on kidney stress were assessed using the Jonckheere-Terpstra test.

Results:

35 (12 Female) patients were included. Median age was 54 years (range 21-76). Median ICU stay was 16 days (range 5-54). Median baseline eGFR-Cr was 96 ml/min/1.73 m2 (range 16-121). 13 patients developed creatinine defined AKI in the first 10 days with 7 receiving kidney replacement therapy (KRT). Distribution of peak TIMP-2.IGFBP-7 within the first 7 days was: Low risk (n=3), Low-Medium Risk (n=11), High-Medium Risk (n=11), High Risk (n=10). Cystatin C eGFR (Median 70ml/min/1.73m2) at discharge was significantly lower than Creatinine eGFR (Median 108) at ICU discharge (P<0.001). No patient remained on KRT at ICU discharge. Peak TIMP-2.IGFBP-7 category correlated with discharge Cystatin C eGFR (P=0.0128), but not correlate discharge Creatinine eGFR (P=0.166), Figure 1.

Discussion:

In critical illness assessment of kidney function using creatinine is confounded by falls in creatinine generation. Here kidney stress was detected in 86% of cases whereas creatinine

defined AKI was observed in 40%. When kidney function was assessed using a measure less-confounded by muscle mass change (Cystatin-c) severity of early kidney stress identified worse kidney function at ICU discharge. This was not observed using Creatinine. TIMP-2.IGFBP-7 may help risk-stratify long term renal function following critical illness. Future evaluation of kidney biomarker tests in critical illness should consider using Cystatin C rather than Creatinine to assess kidney outcomes.

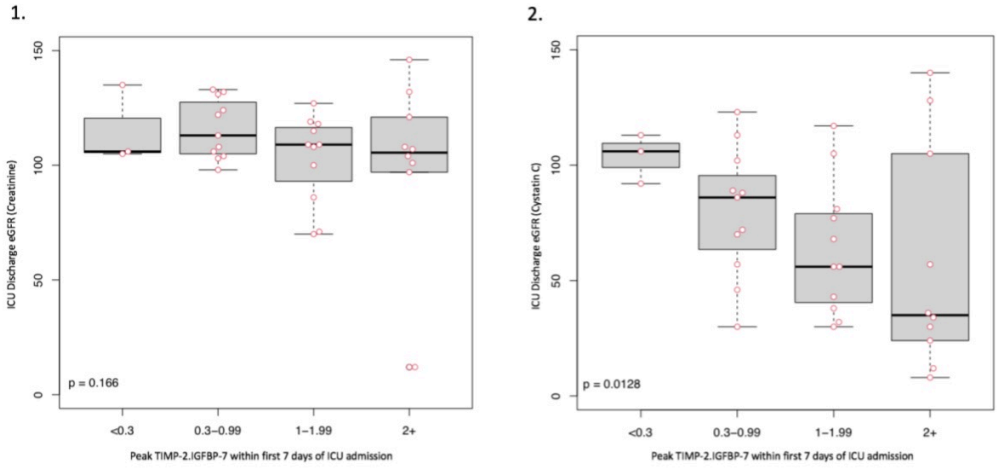

Figure 1: Whisker and Boxplot charts of findings. Charts show peak TIMP-2.IGFBP-7 (Nephrocheck) within first 7 days against ICU discharge eGFR (Creatinine – Chart 1) (Cystatin C – Chart 2). P values shown are based on Jonckheere-Terpstra test for trend.

18

Vitamin B Complex Improves Renal Recovery in Patients with AKI (VIBAKI trial)

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Background: Acute kidney injury (AKI) is a common complication with adverse consequences in hospitalized patients. Preclinical studies have identified that NAD+ augmentation as a potential strategy for the prevention and treatment of AKI. NAD+ is the final metabolized form of vitamin B3. Since there is no availability of vitamin B3 in the country; we tested if I.V. vitamin B complex (vitamin B1, B6 and B12) could improve renal recovery in patients with AKI. By oxidation, vitamin B6 through the pathway of pentose phosphate lead to the formation of NADPH (nicotamide adenine phosphate dinucleotide) an analog of NAD+.
Methods: We conducted randomized, blind, placebo-controlled study in hospitalized patients with AKI(NCT04893733). During the study I.V. vitamin B complex (115 subjects) or placebo (114 subjects) was given twice a day for 5 consecutive days. For AKI management in each patient, a protocol-based approach was used (STOP AKI protocol from the ISN 0by25 trial). Serum creatinine was measured using a POC device (NOVA Biomedical Xpress CREA) at enrollment and every 24 hours for 7 days, and then at day 30, and day 90. We evaluated if vitamin B complex could improve renal recovery in patients with AKI, reduce the risk of de novo CKD or CKD progression, and improve survival.
Results: From September 2020 to September 2021, 300 patients were enrolled in this ongoing RCT with 229 patients completing the follow-up by day 7 and 192 patients completing the follow-up by 3 months. Baseline characteristics are shown on table 1. The drop in sCr values by day 7 was higher in the vitamin B complex group (1.13 vs. 0.35 mg/dl; $p < 0.001$). Complete recovery was higher in patients randomized to vitamin B complex (58.3% vs. 34.5%; p=0.004), no difference was found in terms of partial recovery (27% vs. 29.8%; p=0.850). Non-recovery was lower in patients who received vitamin B complex as compared to placebo (14.8% vs. 36%; p=0.005). At 3 months, the incidence of de novo CKD was not different in both arms (21.7% vs. 28.1%; p=0.113); however, CKD progression was lower in patients who received vitamin B complex (9.6% vs. 20.2%; p=0.009. Ninety-day mortality was higher in patients who received placebo as compare with patients who received vitamin B complex (79.5% vs. 52.5%).
Conclusions: Vitamin B complex could accelerate renal recovery in patients with AKI, reduce CKD progression and improve survival.

Figure on following page

	Vitamin B complex n = 115	Placebo N = 114	*P* value
Age (years)			
Median	71 ± 16	70 ± 16	0,29
Gender, n (%)			
Male	74 (64,3%)	65 (57%)	0,004
AKI KDIGO stage, n (%)			
1	34 (29,6%)	63 (55,3%)	≤0,001
2	42 (36,5%)	28 (24,6%)	≤0,001
3	39 (33,9%)	23 (20,2%)	≤0,001
Baseline sCr and eGFR (CKD-EPI)			
Admission sCr (mg/dl)	2,88 ± 1,4	2,36 ± 1,3	0,006
eGFR (ml/min/1.73 m^2)	64,5 ± 27	61,8 ± 25	0,63
Baseline sCr (mg/dl)	1,49 ± 2,5	1,8 ± 7	0,21
ACR and PCR (spot urine)			
ACR (mg/g)	208 ± 288	374± 675	0,67
PCR (mg/g)	1492 ± 1819	1277 ± 1568	0,52
AKI etiology, n (%)			
Pre Renal	50(43,5 %)	50(43,9%)	0,95
Infection	20 (17,4%)	17(14,9%)	0,61
ATN	8 (7%)	8 (10,1%)	0,46
HRS	5 (4,3%)	5 (4,4%)	0,98
CRS	7 (6,1%)	8 (7%)	0,77
Nephrotoxins	8 (7 %)	8 (7%)	0,98
Obstructive	4 (3,5%)	3 (2,6%)	0,71
Herbal medicines	4 (3,5%)	3 (2,6%)	0,71
AIN	2 (1,7%)	4 (3,5%)	0,41
Glomerulonephritis	7 (6,1%)	4 (3,5%)	0,36
Nephrotoxins, n (%)			
PPI	16 (13,9%)	26 (22,8%)	0,076
ARBs	20 (17,4%)	25 (21,9%)	0,387
NSAIDs	11 (9,6%)	14 (12,3%)	0,495
ACEs	4 (3,5%)	8 (7%)	0,229
Comorbidities, n (%)			
Age >65 years	81 (70,4%)	84 (73,7%)	0,584
Chronic cardiac disease	41 (35,7%)	42 (36,8%)	0,851
Type 2 diabetes mellitus	35 (30,4%)	42 (36,8%)	0,305
Cancer	20 (17,4%)	20 (16,5%)	0,976
Anemia	26 (22,6%)	37 (32,5%)	0,095
Chronic kidney disease	28 (34,6%)	17(21,5%)	0,292
Dehydration	19 (16,5%)	12 (10,5%)	0,185
Chronic pulmonary disease	18 (15,7%)	18 (15,8%)	0,977

Abstract Category: B) Research in AKI

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Persistent Serum Renin Elevation is Associated with Acute Kidney Injury in Pediatric Septic Shock

Natalja L Stanski[1], Naomi Pode Shakked[1], Hector R Wong[1], Stuart L Goldstein[1]

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STUDY PURPOSE: Sepsis-associated acute kidney injury (SA-AKI) is associated with significant morbidity and mortality in critically ill children. Unfortunately, its pathophysiology is poorly understood, limiting treatment strategies. Adult studies highlight the potential role of the renin-angiotensin-aldosterone system (RAAS), by correlating renin levels >59 pg/ml with development of AKI in vasodilatory shock. This concept has not yet been examined in children.

METHODS: A secondary analysis of 379 children admitted to a PICU from a multi-center study of pediatric septic shock. A subset of 69 patients were selected based on availability of Day1 (D1) and Day3 (D3) serum samples, and the presence or absence of D3 severe SA-AKI (primary outcome, defined as ≥KDIGO stage 2). Serum renin concentrations were measured on D1 and D3 by Luminex assay; these values, and their trend (D3:D1 ratio), were assessed for associations with SA-AKI and provision of renal replacement therapy (RRT). Risk stratified analyses were also performed using the previously validated Renal Angina Index (RAI) and the recently derived PERSEVERE-II Model.

RESULTS: 26/69 (38%) subjects developed D3 severe SA-AKI and 12 (17%) received RRT. Median D1 renin value was 4751 pg/ml (IQR 1926-10307), with no D1 differences between subjects with vs. without D3 severe SA-AKI or RRT requirement. Median D3 renin values were higher for those with D3 severe SA-AKI (5250 pg/ml vs. 2153 pg/ml, p=0.035) and those who required RRT (7514 pg/ml vs. 2221 pg/ml, p=0.014). These subjects also had higher median D3:D1 renin ratios (D3 severe SA-AKI: 0.99 vs 0.41, p=0.003; RRT: 1.1 vs. 0.51, p=0.014). In patients at high risk for D3 severe SA-AKI by either the RAI or the PERSEVERE-II Model, the median D3:D1 renin ratio discriminated between true positives (those who developed severe SA-AKI) and false positives (those who did not) (RAI: 0.99 vs 0.41, p=0.016; PERSEVERE-II: 0.95 vs 0.41, p=0.023).

CONCLUSIONS: Children with septic shock have very elevated renin levels on presentation, and persistent elevation at D3 is associated with severe SA-AKI and provision of RRT. This persistence also discriminates between true positives and false positives in high-risk patients identified by existing SA-AKI predictive tools. These data suggest a potential role of RAAS in SA-AKI pathophysiology that should be further explored.

Abstract Category: B) Research in AKI

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Trajectories of urinary C–C motif chemokine ligand 14 (CCL14) and the persistence of severe acute kidney injury during critical illness

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Background: In critically ill patients with established stage 2-3 acute kidney injury (AKI) elevated urinary C-C-motif chemokine ligand 14 (CCL14) has been shown to predict persistence of severe kidney injury [1,2], however the relationship of CCL14 trajectory to persistent severe AKI has not been described.

Methods: Using existing data from two multicenter studies (Ruby and Sapphire) in mixed populations of critically ill adults, we analysed 3 consecutive measurements of urinary CCL14 at 12-hour intervals after development of moderate to severe AKI. CCL14 concentrations were measured using the NEPHROCLEAR™ CCL14 Test on the Astute 140® Meter (Astute Medical Inc., San Diego, CA). Primary endpoint was the development of persistent severe AKI (PS-AKI): 72 consecutive hours of stage 3 AKI or death or receipt of dialysis prior to 72h. We hypothesised that, trajectories of urinary CCL14 would provide additional information as to the likelihood of PS-AKI over the initial measurement. We stratified the CCL14 concentrations into three levels: Low (≤1.3 ng/mL), Medium (>1.3 to ≤13 ng/mL), and High (>13 ng/mL) based on previously determined clinical-risk cutoffs [3], and grouped patients by the pattern of CCL14 levels across the 3 samples.

Results: We included 417 patients (Median age 65, 59% male) with 3 consecutive CCL14 measurements, of which 75 developed PS-AKI. Initial CCL4 levels were low in 196 (47%), medium in 180 (43%) and high in 41 (9.8%). As previous described [3] initial CCL14 category strongly correlated with primary endpoint, and in a majority of cases (66%) CCL14 category was unchanged from first to last timepoint (Figure). In multivariable logistic regression, accounting for initial CCL14 category, a decrease in CCL14 category in the first 24h was associated with decreased risk of PS-AKI, odds ratio (OR) 0.2 (95% CI 0.08 – 0.45, $p < 0.001$) and an increase in category with increased risk, OR 4.04 (1.75 – 9.46, p=0.001).

Conclusions: In two-thirds of patients with moderate to severe AKI, CCL14 levels were stable over a 24h period, and where changes occurred these correlated with risk level for PS-AKI. Clinicians can have confidence in the prognostic interpretation of a single CCL14 result, but serial measurement may reveal dynamic pathology and help refine prognosis over time.

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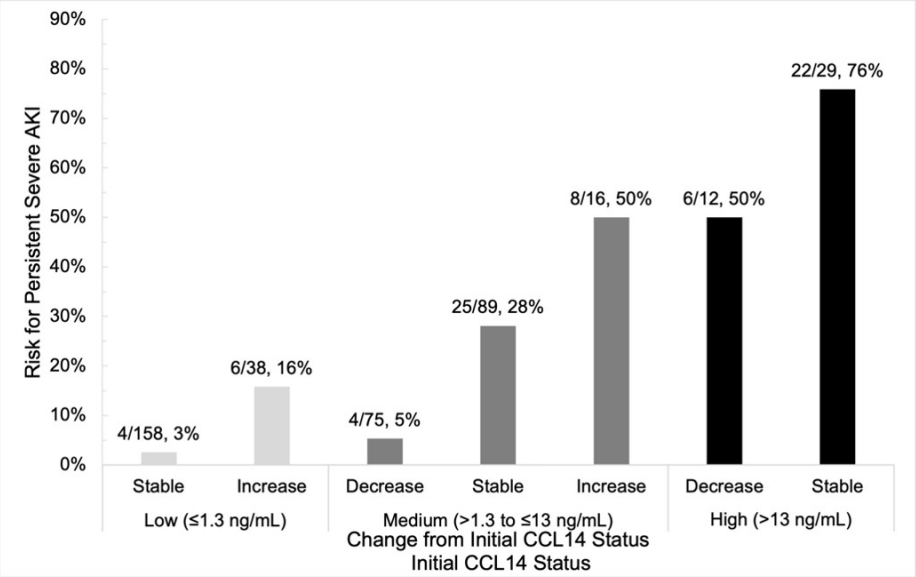
2. Bagshaw, S.M, 2021. Critical Care, 25:1-8.
3. Koyner, J.L, 2021. Manuscript submitted for review.



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Role of tissue inhibitor of metalloproteinases-2 and insulin like growth factor binding protein 7 for early recognition of acute kidney injury in critically ill COVID-19 patients

GUSTAVO CASAS[1], SANTIAGO AVILA-RIOS[1], ISABEL LEON-ROGRIGUEZ[1], DAVID ESCAMILLA[1], NATALIA CALDERON[1]

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Background: A high proportion of critically ill patients with COVID-19 develop AKI and die. Early recognition of subclinical AKI could contribute to AKI prevention. Therefore, this study was aimed at exploring the role of the urinary biomarkers NGAL and [TIMP-2]•[IGFBP7] for early detection of AKI in this population.

Methods: This prospective, longitudinal cohort study included critically ill COVID-19 patients without AKI at study entry. Urine samples were collected on admission to critical care areas for determination of NGAL and [TIMP-2]•[IGFBP7] concentrations. Demographic information, comorbidities, clinical and laboratory data were recorded. The study outcomes were development of AKI and mortality during hospitalization. Comparisons of individuals who developed AKI during hospitalization vs. those without AKI were made using chi-squared test for categorical variables and Mann-Whitney U for continuous variables. Urinary biomarkers and their cutoff values were selected based on the highest sensitivity, specificity and area under the receiver-operating characteristics curve with 95% confidence intervals for prediction of AKI. Selected biomarkers and cutoffs were used in the Kaplan-Meier survival analyses for the time to AKI. Logistic regression analysis was used to identify the association between relevant covariates with AKI and mortality. For all analyses, two-sided P values <0.05 were considered statistically significant.

Results: Of the 51 individuals studied, 25 developed AKI during hospitalization (49%). The risk factors for AKI were male gender (HR=7.57, 95% CI: 1.28-44.8; p=0.026) and [TIMP-2]•[IGFBP7] > 0.2 (ng/ml)2/1000 (HR=7.23 , 95% CI: 0.99-52.4; p=0.050). Mortality during hospitalization was significantly higher in the group with AKI than in the group without AKI (p=0.004). Persistent AKI was a risk factor for mortality (HR=7.42, 95% CI: 1.04-53.04; p=0.046).

Conclusions: The combination of [TIMP-2]•[IGFBP7], together with clinical information, were useful for identification of subclinical AKI in critically ill COVID-19 patients. The role of additional biomarkers and their possible combinations for detection of AKI in critically ill COVID-19 patients remains to be explored in large clinical trials.

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A Critical Appraisal of Clinical Practice Guidelines on Acute Kidney Injury Using the AGREE II Instrument

Background & Purpose of the Study: Acute kidney injury (AKI) is strongly associated with increased morbidity and mortality. Management of AKI, globally is highly variable due to knowledge-to-action gaps and inconsistent access to resources. Clinical practice guidelines can provide important guidance and, when evidence warrants strong recommendations, can help to minimize variability in care; however, evaluating the trustworthiness of recommendations requires appraisal of guideline quality. The objective of this systematic survey is to critically appraise clinical practice guidelines (henceforth referred to as guidelines) addressing management of AKI. We also examined the differences and agreement between guideline recommendations.

Methods: We systematically searched MEDLINE, the National Guideline Clearinghouse, Guideline International Network, and Turning Research into Practice, without language restrictions. Guidelines that address diagnosis, monitoring or management of AKI in adult or pediatric populations were eligible for our review. We excluded guidelines addressing prevention of AKI and those specific to kidney transplant recipients.
Teams of two reviewers, independently and in duplicate, screened titles and abstracts and potentially eligible full text reports to determine eligibility, and appraised the reporting quality of AKI guidelines using the Advancing Guideline Development, Reporting and Evaluation in Health Care instrument II (AGREE). The AGREE II instrument (www.agreetrust.org) contains 23 items divided into six domains: scope and purpose; stakeholder involvement; rigour of development; clarity of presentation; applicability; and editorial independence. A seven-point scale is used to answer each question with a range of options from 1 (strongly disagree) to 7 (strongly agree).
We calculated standardized scores ranging from 0% to 100% for each domain.

Results: Eleven guidelines published from 1997 to 2016 addressing the diagnosis, monitoring or management of AKI proved eligible. Two guidelines included recommendations on nutrition in AKI. Only one guideline made recommendations for the pediatric patient population. The NICE and KDIGO guidelines performed best with respect to AGREE II criteria; only one other guideline warranted high scores on three domains.

Conclusions: Only two of these guidelines, the KDIGO and NICE guidelines, met most criteria of the AGREE II instrument.

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Short-term Outcomes of Patients with Severe Acute Kidney Injury in an Intensive Care Unit of a Low-middle Income Country

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Background: Severe acute kidney injury (AKI) is associated with substantial short-term and long-term mortality. While extensively described in developed countries, the short-term and long-term outcomes of severe AKI, particular AKI required renal replacement therapy (RRT), have not been well reported in resource-limited countries. The aim of this study was to evaluate the short-term outcomes of severe AKI and the impacts of RRT modalities on mortality in a low-middle income country.

Methods: This was a prospective observational study conducted in two intensive care units of a tertiary hospital in Viet Nam from 7/2019 to 7/2021. Patients diagnosed with severe AKI according to KDIGO criteria were enrolled and monitored until discharge, then followed up every 3-month. We performed multivariate Cox regression analysis to identify the independent factors associated with mortality. The Kaplan-Meier method was used to estimate the overall survival probability, stratified by modalities of RRT.

Results: A total of 308 patients were included, 61% of the patients were male. 281 patients (91.2%) were treated with all RRT, and 81/281 patients (28.8%) were switched from initial mode to another mode of RRT. The mortality rates at hospital discharge and at 6-month were 34% and 60%, respectively. There were no significant differences in the 6-month mortality amongst the patients initially treated with CRRT, IHD or SLED (p=0,324). Postoperative complications [HR 2,14 (1,4 – 3,29), p<0.001], septic AKI [HR 1,93 (1,15-3,23), p=0,013] and vasopressor treatment in 28 days [2,73 (1,37-5,44), p=0.004] were independently associated with 6-month mortality.

Conclusions: Our study demonstrates that severe AKI in the ICU is associated with worsen 6-month mortality. While postoperative complications, septic AKI, and vasopressor treatment were independent factors of death, initial modalities of RRT do not change patients' survival rate.

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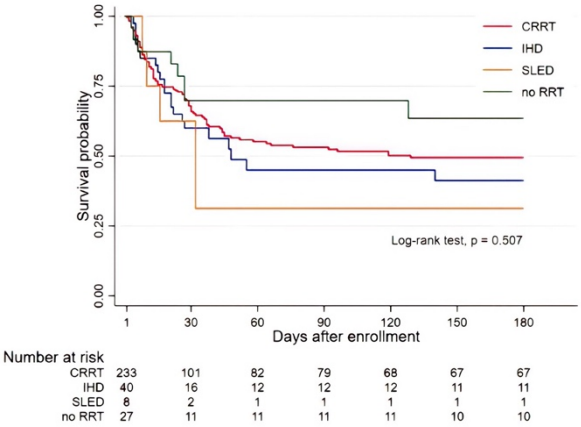

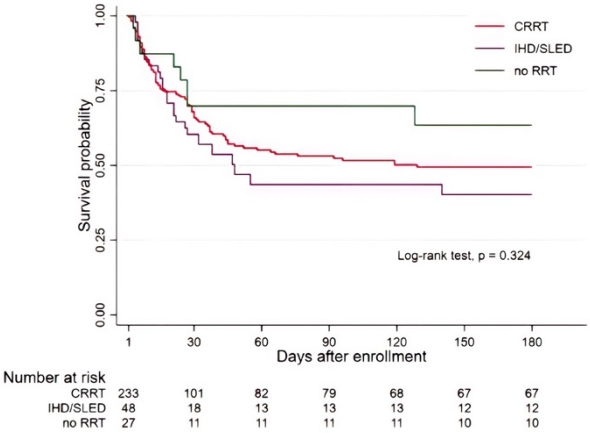

Abstract Category: B) Research in AKI

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Proteomic analysis indicates increased expression of extracellular matrix proteins in the kidneys of mice following acute kidney injury

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Introduction: Acute kidney injury (AKI) can result in kidney fibrosis. Common methods to assess kidney fibrosis include Picrosirius Red or Trichrome staining, and immunohistochemical staining for type 3 collagen. Proteomics – a method of measuring all protein expression levels within a sample – represents a more robust and comprehensive method of quantifying fibrosis. Proteomics by liquid chromatography tandem mass spectrometry (LC-MS/MS) offers thorough analysis into changes to the kidney extracellular matrix (ECM), but previous studies fail to capture the ECM proteome in depth. Here, following an ECM-targeted extraction protocol, we perform LC-MS/MS on AKI vs. sham kidneys to determine changes to the ECM following AKI.

Methods: All procedures were IACUC approved. 8 week-old C57BL/6J male mice underwent bilateral ischemia-reperfusion kidney injury (clamp duration 25 minutes); sham controls underwent the same procedure sans renal pedicle clamping. After 3 months, animals were euthanized, kidneys harvested, processed for ECM extraction, and the resulting samples (N = 3 for each AKI and sham) were analyzed by LC-MS/MS. Bioinformatics and machine learning methods were performed on the resulting dataset. Statistical significance of proteins was determined by FDR corrected t-test p-value < 0.05.

Results: Hierarchical clustering and principal component analysis (not shown) demonstrates separation of AKI and sham by their ECM proteomes. Proteins expressed at high levels in AKI kidneys include PRELP, BGN, ECM1, LUM, MATN2, and OGN which all contribute to ECM anchoring; collagen, fibrillar, or filament assembly; or ectopic calcification. Strong correlations between AKI and the ECM proteins COL1A, COL3, TNC, and FGG were also identified. MATN2 and TNC (involved in ECM and tissue formation) were identified as top proteins contributing to AKI injury status.

Conclusions: Here we identify important changes to the kidney ECM following ischemia-reperfusion AKI. These data suggest an increase in tissue ECM production, especially fibrillar collagens and ECM assembly 3 months after AKI, findings which are corroborated throughout the literature. Future studies will investigate different timepoints, changes in cell response (qPCR), and mining these data for differences in other hallmark proteins involved in fibrosis and in the progression of AKI disease.

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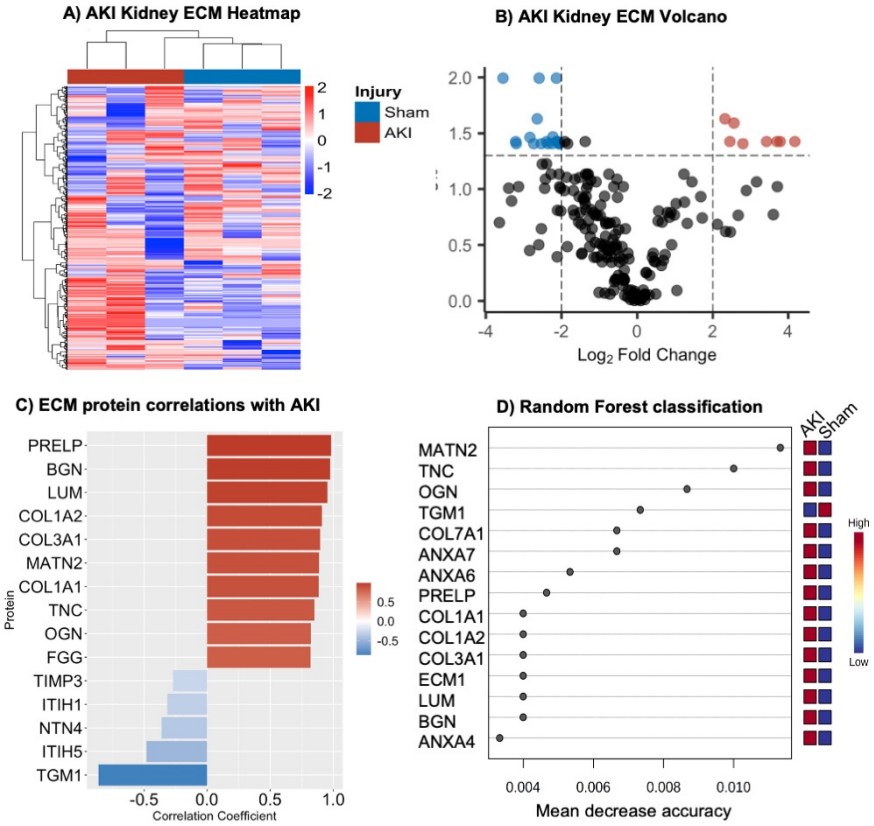

Proteomics analysis between the ECM of kidneys having sustained AKI compared to sham kidneys (no injury). Proteomic profiles between AKI (red) and Sham (blue) demonstrate A) clustering by group, B) high expression of certain proteins (red/blue dots) by each group, and C) proteins with high positive correlation (red) and negative correlation (blue) with AKI. D) Random forest analysis showing the top 15 proteins contributing to the classification of kidney ECM samples towards AKI or sham.

Abstract Category: B) Research in AKI

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Utility of 8 hour Urine Creatinine Clearance to Guide Dosing in Critically Ill Patients: A Single Centre Retrospective Analysis

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[1]*Guy's and St Thomas´ NHS Foundation Trust*

Introduction
Serum creatinine (SCr) is used to calculate Cockcroft-Gault Creatinine Clearance (C&G CrCl) to estimate Glomerular Filtration Rate (GFR) and guide drug dosing (1). However, SCr is reported to have low sensitivity for detecting renal dysfunction in critical illness. Population based equations such as C&G CrCl have not been validated in Acute Kidney Injury (AKI), secondary to induced pathophysiological changes. Direct measurement of CrCl is advocated such as 4-8hr Urine Creatinine Clearance (UrCrCl) (1). In this retrospective analysis we describe the variation in estimated GFR (eGFR) from results of C&G CrCl, CKD-EPI eGFR and measured UrCrCl.

Method
Retrospective data collection and case note review from electronic health records (Phillips ICCA® and iSOFT Clinical Manager®) was completed from Dec 2018 to Nov 2021, for patients admitted to adult critical care at Guy's and St Thomas' Foundation Trust who had a measured UrCrCl measured. The aims were to compare results and to assess the impact on drug dosing.

Results
In 28/31 (90.3%) patients, C&G CrCl was an over-estimation of renal function, with a median difference between C&G CrCl and measured UrCrCl of 239%. UrCrCl results triggered a change in drug dosing in 16/31 (51.6%) of patients. Drug dosing could have been optimised in a further 7/31 (22.6%) patients if the UrCrCl results had been noticed and acted upon within 24hrs (Table 1).

Conclusion
UrCrCl provides a more accurate measure of GFR compared to C&G CrCl or eGFR and triggered a change in drug therapy in 52% of patients. UrCrCl is useful in patients in whom serum creatinine results may be confounded by extremes of age, frailty, low muscle mass and fluctuations in fluid balance. Thus, UrCrCl results serve to optimise drug dosing and limit risks of harm from both, toxicity and underdosing.

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Patient characteristics (n=31)	Results
Median age	48 yrs
Median SCr [micromole/L]	56 (IQR 27-104.5)
Median C&G CrCl [ml/min]	109 (IQR 41 – 244)
Median eGFR [ml/min]	104 (IQR 52 – 236)
Median UrCrCl [ml/min]	39 (IQR 15-75)
Median % difference between C&G CrCl and UrCrCl	239% (IQR 134% - 415%)
UrCrCl result prompted change of drug therapy	51.6% (16/31)

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Serum Potassium Trajectory During AKI and Mortality Risk

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Introduction: Kidneys play a primary role in potassium homeostasis. The association between potassium (sK+) level and mortality or the need for kidney replacement therapy (KRT) during acute kidney injury (AKI) has not been adequately explored.

Methods: In this prospective cohort study, AKI patients admitted to the Hospital Civil de Guadalajara were enrolled from August 2017 to June 2021 with AKI. We divided patients into 8 groups based on the serum potassium level trajectories up to ten days following hospitalization, (1) normokalemia (normoK), defined as sK+ values between 3.5 and 5.5 mEq/L; (2) corrected hyperkalemia (hyperK), sK+ > 5.5 mEq/L on hospital admission and decreased to normoK; (3) corrected hypokalemia (hypoK), sK+ < 3.5 mEq/L on hospital admission and increased to normoK; (4) fluctuating potassium, sK+ increased / decreased in and out of normoK parameters; (5) uncorrected hypoK, sK+ < 3.5 mEq/L; (6) normoK to hypoK, sK+ that were normal on hospital admission and decreased to hypoK and never went back to normal; (7) normoK to hyperK, sK+ that were normal on hospital admission and increased to hyperK and never went back to normal; (8) uncorrected hyperK, sK+ > 5.5 mEq/L. We assessed the association of serum potassium trajectories with mortality and the need for KRT (secondary objective).

Results: A total of 311 AKI patients were included. The mean age was 52.6 years, and 182 (58.6%) were male. AKI stage 3 was present in 199 (63.9%). KRT started in 112 (36%) patients, and 66 (21.2%) died. After adjusting for confounders, 10-day hospital mortality was significantly higher in group 7 and 8 (OR, 1.37 and 1.63, p = <0.05, for both, respectevely), and KRT initiation was higher only in group 8 (OR 1.40, p = < 0.05) compared with group 1. Mortality in different subgroups of patients in group 8 did not change the primary results.

Conclusion: In our prospective cohort, most patients with AKI had alterations in + sK . NormoK to hyperK and Uncorrected hyperK were associated with death, while only uncorrected hyperK was correlated with the need for KRT.

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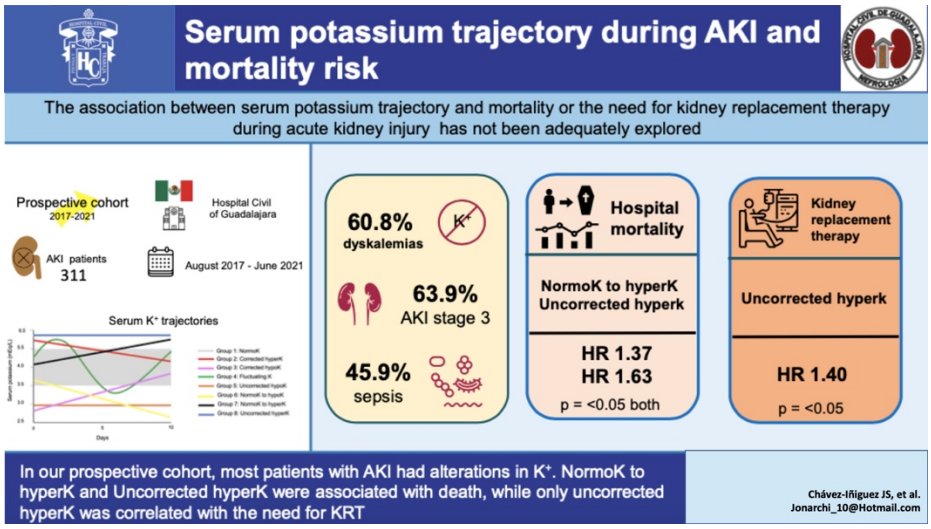

Abstract Category: B) Research in AKI

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SerpinA3 in Predicting Renal Recovery from Acute Kidney Injury in Critically COVID-19 Patients

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Background: Numerous studies have suggested a possible role for acute kidney injury (AKI) biomarkers in predicting renal recovery after renal replacement therapy (RRT). In the context of AKI secondary to COVID-19 disease, little has been explored. Nonrecovery of renal function carries to significant negative effects. We recently reported that the urinary excretion of Serpin-A3 (uSerpA3) is an early marker of renal injury and fibrosis. In this study, we investigated uSerpA3 as a biomarker for predicting renal recovery following AKI in critical ill COVID-19 patients on invasive mechanical ventilation (IMV).

Methods: Prospective cohort study of COVID-19 patients in ICU on IMV and requirement of RRT, admitted to our Institute in Mexico City (Mar 2020 - Mar 2021). Patients with CKD stages 4 or 5 and kidney transplant were excluded. Urinary serpinA3, KIM-1 and HSP-72 as renal injury biomarkers were measured in urine on day 0 (RRT start) and days 1, 3, 7 and 14. We analyzed their predictive ability for subsequent recovery, defined as alive and independent from dialysis at 90 days.

Results: We included 54 patients, 41 (76%) patients were male and the median of age was 54 years (IQ 43-62). Twenty-eight patients (52%) died, all patients who lived only 48% recovered kidney function after 90 days. KIM-1 on day 0 (when RRT start) was predictor of renal recovery however, it has a high rate of false positives (65% sensitivity and false positive rate of 38%). uSerpA3 on day 7, was an accurate predictor of renal recovery, the best area under the receiver-operating characteristics curve (AUC) (AUC 0.72, 95% CI 0.51-0.94). None of the HSP-72 measurements predicted renal recovery.

Conclusions: In this study, we found that uSerpA3, a novel urinary biomarker, is useful to predict recovery at 90 days after a severe AKI episode that required RRT in critically ill Covid-19 patients.

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Urinary biomarker	Time point	AUC	95% CI	p value
SerpinA3	Day 0	0.51	(0.32-0.70)	0.92
	Day 1	0.61	(0.42-0.80)	0.29
	Day 3	0.61	(0.40-0.83)	0.29
	Day 7	0.72	(0.51-0.94)	0.04
	Day 14	0.73	(0.48-0-98)	0.13
HSP-72	Day 0	0.49	(0.28-0.69)	0.90
	Day 1	0.58	(0.38-0.78)	0.43
	Day 3	0.56	(0.35-0.77)	0.60
	Day 7	0.60	(0.39-0.81)	0.37
	Day 14	0.43	(0.48-0.98)	0.08
KIM-1	Day 0	0.71	(0.54-0.88)	0.04
	Day 1	0.60	(0.40-0.80)	0.32
	Day 3	0.61	(0.40-0.82)	0.33
	Day 7	0.57	(0.35-0.79)	0.11
	Day 14	0.49	(0.23-0.76)	0.58

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Serum Renin Levels Refine Acute Kidney Injury Prediction in Critically Ill Children

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[1]*Cincinnati Children's Hospital Medical Center*

Purpose: Acute kidney injury (AKI) is common in the pediatric intensive care unit (PICU) and portends an increased risk for poor outcomes, including death. Unfortunately, treatments are limited, and thus early risk stratification of children for severe AKI (sAKI) is important, as it could facilitate targeted, renal protective interventions. Recent adult studies have demonstrated a correlation between early elevation in serum renin level and development of sAKI. We sought to assess whether similar associations exist in children.

Methods: We performed a prospective pilot study of children admitted to the PICU and enrolled in the Trial in AKI using NGAL and Fluid Overload to Optimize CRRT Use (TAKING FOCUS 2, NCT03541785; Figure 1). All patients enrolled had a Renal Angina Index (RAI) calculated at 12 hours of PICU admission and urine neutrophil gelatinase-associated lipocalin (uNGAL) measured if RAI≥8 (high risk sAKI= RAI≥8 and uNGAL ≥150 ng/ml). 43 patients were enrolled in our study. We assessed for associations between renin levels (both alone and in concert with the RAI/uNGAL paradigm) and our primary outcomes of Day2-4 sAKI (≥KDIGO stage 2) and receipt of renal replacement therapy (RRT). Response to a furosemide stress test (FST) was a secondary outcome.

Results: 21/43 (49%) patients had Day2-4 sAKI and 8/43 (19%) received RRT. Median Day1 renin level was 59.6 pg/ml (IQR 21,128), and there were no differences between patients with and without either primary outcome. An optimal cutoff for Day1 renin of 100 pg/ml was identified to discriminate between patients with and without Day2-4 sAKI (Youden Index 0.2). Although Day1 renin alone was poorly correlated with both primary outcomes, patients with RAI≥8 had higher Day1 renin levels compared to those with RAI<8 (median 72.3 vs. 21.6 pg/ml, $p<0.05$). When Day1 renin ≥100 pg/ml was added to the RAI/uNGAL sAKI prediction paradigm (Figure 1), specificity of Day2-4 sAKI (82% vs. 59%) and RRT use (74% vs. 44%) prediction improved. Finally, 12 patients underwent FST, and median Day1 renin levels discriminated between responders (n=8) (101 pg/ml, IQR 32,485) and non-responders (n=4) (537 pg/ml, IQR 95,2182).

Conclusions: Elevated Day1 renin level may refine sAKI risk stratification when integrated with the RAI and uNGAL. Elevated renin levels also appear to identify FST non-responders who may benefit from earlier RRT. Further study is warranted to validate these findings.

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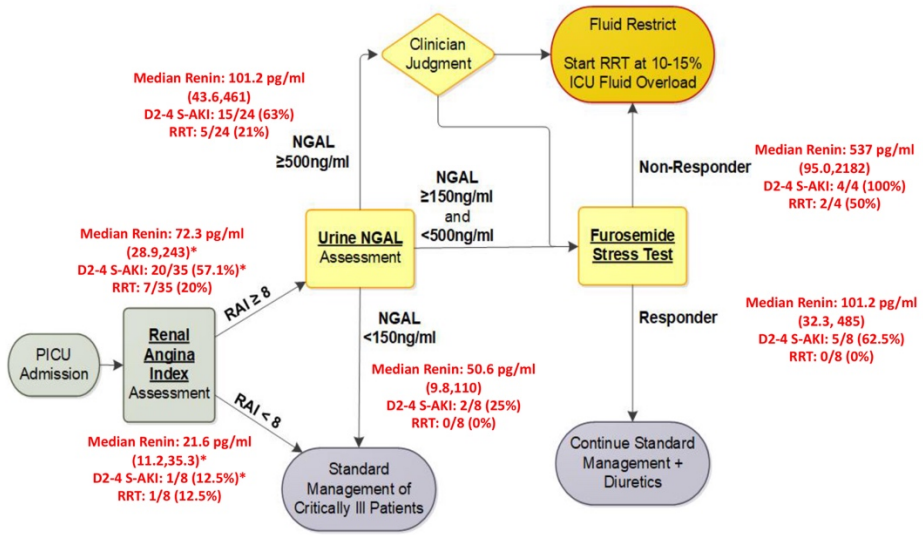

Figure. 1. Use of Renal Angina Index (RAI) and urine NGAL (uNGAL) assessment to predict severe AKI (sAKI) and guide fluid management as part of the Trial in AKI using NGAL and Fluid Overload to optimize CRRT Use (TAKING FOCUS 2, NCT 03541785). Median, 25th and 75th percentile of serum renin levels as well as percentages of D2-4 sAKI and need for RRT for each branch point are presented in red.

Abstract Category: B) Research in AKI

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A predictive model for sepsis-associated acute kidney injury in mice

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Objective:
The pathophysiology of sepsis-associated acute kidney injury (SA-AKI) is incompletely understood but likely distinct from other forms of AKI and primarily related to the inflammatory state induced by sepsis. mPERSEVERE is a sepsis-related murine biomarker panel that has been shown to reliably predict 10-day mortality after induction of sepsis. The aim of this study is to interrogate the mPERSEVERE biomarker panel to determine if cytokines or chemokines within the panel play a role in the pathogenesis of SA-AKI.

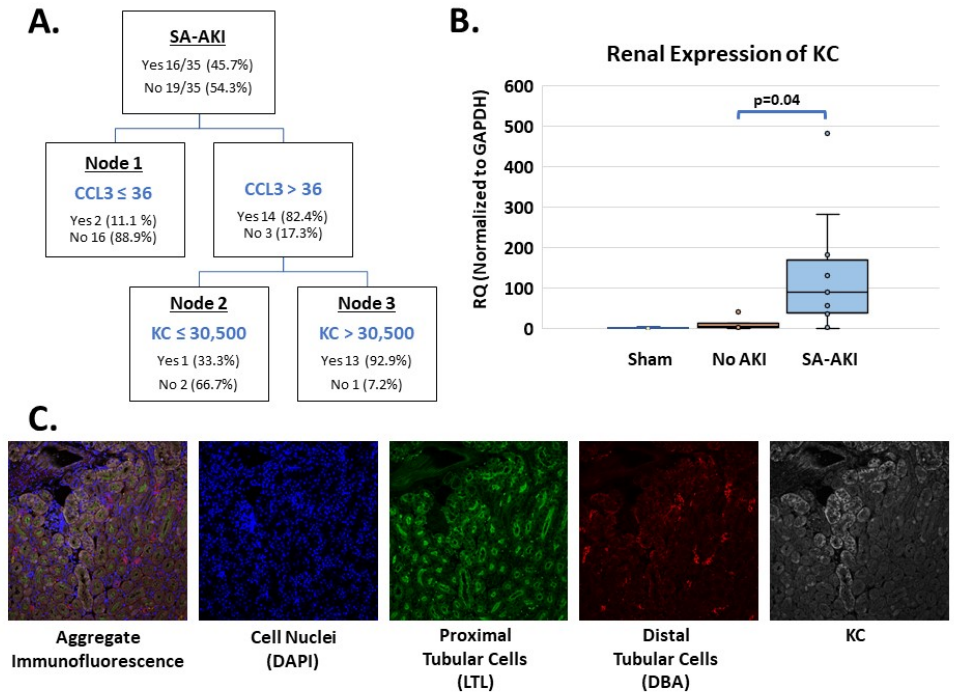
Methods:
Eight-week-old C57BL/6 male mice underwent induction of sepsis by cecal ligation and puncture (CLP). mPERSEVERE plasma biomarkers were collected at 8-hours and used to develop a model to estimate the risk of developing SA-AKI at 24-hours. We measured serum creatinine and harvested kidneys at 24-hours. Gene expression levels of biomarkers were quantified using quantitative polymerase chain reaction (qPCR) from whole kidneys, and immunofluorescence was used to localize biomarkers within the kidney using lotus tetragonolobus lectin (LTL) to highlight proximal tubule cells and dolichos biflorus agglutinin (DBA) to highlight distal tubule cells.

Results:
Using classification and regression tree analysis, a SA-AKI predictive model was generated using two mPERSEVERE biomarkers: C-C motif chemokine ligand 3 (CCL3) and keratinocyte-derived chemokine (KC); area under the curve (AUC)=0.90 (Fig 1A). 48 mice underwent CLP; 23 (47.9%) stratified as high-risk (HR) for SA-AKI and 25 (52.1%) as low-risk (LR). Of HR mice, 68% developed SA-AKI at 24-hours compared to 13% of LR mice ($p<0.001$). In mice with SA-AKI, renal expression of KC but not CCL3 was increased compared to mice without SA-AKI ($p=0.04$) (Fib 1B). KC co-localized with lotus tetragonolobus lectin to the renal proximal tubule cells (Fig 1C).

Conclusions:
The combination of CCL3+KC reliably estimates SA-AKI development in mice at 24-hours following CLP. KC demonstrated increased expression in mice that develop SA-AKI and localized to the proximal tubule cells by immunofluorescence. KC is a candidate for future SA-AKI mechanistic studies.

Fig 1 A) A predictive model for murine SA-AKI generated using mPERSEVERE biomarkers. Nodes 1 & 2 predict No AKI, Node 3 predicts SA-AKI. B) Renal expression of KC at 24-hours

post-CLP, normalized to GAPDH. C) In a mouse with SA-AKI, immunofluorescence co-localizes KC to renal proximal tubular cells via LTL rather than to distal tubules (20x).



Abstract Category: B) Research in AKI

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Artemisinin ameliorates cisplatin-induced acute kidney injury via inhibiting NF-κ B activated pyroptosis pathways

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Aims: Cisplatin is one of most effective chemotherapy regimens that serves a pivotal role in human cancer treatment; however, it leads to nephrotoxicity in 20-50% of patients. We aimed to investigate the potential preventative role of artemisinin (ARS) pre-treatment and its regulating mechanisms in mice with cisplatin induced acute kidney injury (AKI).

Methods: Male mice at 8-9 weeks were randomly divided into three groups. The "ARS + cisplatin" ("AC", n = 6) mice were treated with 100mg/kg/day of ARS via intragastric gavage (ig) for 4 days following with administration of ciaplatin (20 mg/kg/day) through intraperitoneal (ip) injection for 3 days. The cisplatin group of mice ("CP", n = 6) were treated with the vehicle solution (0.5% carboxymethylcellulose) followed by the same procedure of cisplatin like the "AC" group. The control ("Ctrl", n = 6) mice were subjected for 4 days of 0.5% carboxymethylcellulose and 3 days of saline solution. Mice were sacrificed 72 hours post the treatment. Kidney tissues were collected for periodic Acid-Schiff stain (PAS) and western-blot (WB) assays. Blood samples were used for testing serum creatinine (Scr) and blood urea nitrogen (BUN).

Results: The "CP" mice displayed slightly severer AKI related pathological changes inflammatory cell infiltration than "AC" group. The Scr and BUN levels of "AC" mice are significantly lower ($p = 0.0035$ and 0.0205, respectively) than "CP". Compared with "CP" group, "AC" mice gained remarkably lower ($p < 0.0001$) tubular injury scores via PAS assay. Taken together, our results demonstrated that an improved renal function (RF) was found under the condition of ARS pre-treatment. As previous studies suggested that cisplatin-induced kidney toxicity can be attenuated via inhibiting the NF-κB pathway, we therefore selected and detected 7 key regulators include NLRP3, p65, phosphorylated-p65 (p-p65), Iκbα, phosphorylated-Iκbα(p-Iκbα), GSDMD and N-terminal active fragment of GSDMD (GSDMD-N) to investigate their roles in ARS-related RF improvement. We observed an decreased expression of NLRP3, p65, p-p65 and GSDMD-N, an increase of Iκbα and p-Iκbα, and non-significant change of GSDMD in "AC" mice, suggesting the NF-κB activated pyroptosis pathways were suppressed by ARS.

Conclusion: Our results indicated that ARS pre-treatment is a potential administration to ameliorate cisplatin induced renal injury.

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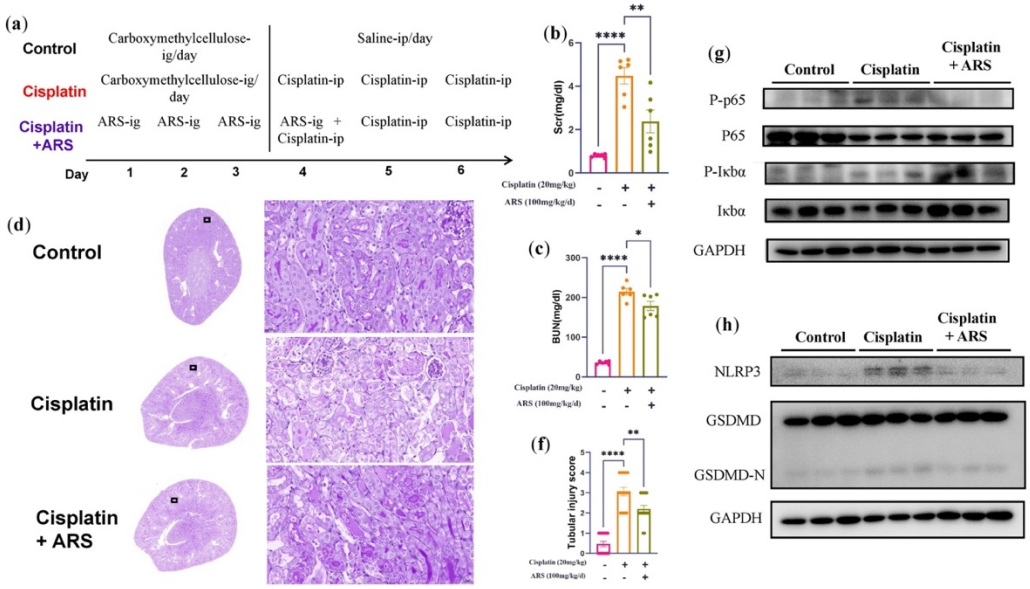

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Kidney Tubular AMP-activated protein kinase (AMPK) Activation is Protective Against Sepsis-associated Acute kidney Injury

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Introduction: Sepsis-associated acute kidney injury (S-AKI) is a life-threatening complication associated with high mortality. We and others have demonstrated that treatment with pharmacologic agents known to activate AMPK decreases the development of S-AKI and improves survival in a rodent model of sepsis. Our preliminary data suggest knockout of AMPK in immune cells decreases the protective effect of pharmacologic AMPK activation against AKI. However, it is still unclear what the role of kidney AMPK activation is in the protection against AKI during sepsis. We hypothesized that activation of AMPK in tubule epithelial cells (TEC) protects against the development of AKI through a tolerance mechanism.

Methods: We created a novel conditional, kidney tubule-specific knockout system, the AMPKα1flox/floxα2flox/flox/Pax8-rTA/LC1. AMPK KO and wild-type (WT) littermates were treated with doxycycline (2mg/ml doxycycline, 5% sucrose in water x 3 weeks) to induce KO of AMPK in TEC. Mice were then randomized to treatment with the AMPK activator AICAR (500mg/kg/IP) 24 hours before cecal-ligation and puncture (CLP) or no treatment(n=6-20/group). TEC AMPK KO was confirmed using PCR and the following outcomes were measured at 24 h: kidney injury measured using the increase in serum creatinine (Cr) from baseline to 24h post-CLP, survival, and peritoneal bacterial colony-forming units (CFU) in peritoneal lavage fluid (PLF).

Results: AMPK knockout in TEC was confirmed using PCR of kidney tissue (Fig1A). KO animals had a higher increase in Cr at 24 hours when compared to WT. Treatment with AICAR limited the elevation of creatinine after CLP in both KO and WT animals (Fig1B). KO animals showed a trend toward lower survival, however, treatment with AICAR had a trend to improve survival in both groups (Fig1C). There was no difference in the peritoneal bacteria CFU between groups (Fig1D).

Conclusion: Activation of constitutionally expressed AMPK in TEC is protective against AKI and possibly, against death during sepsis. Protection against AKI induced by AICAR appears to operate through a tolerance mechanism. However, this protection was not dependent on kidney TEC AMPK expression, suggesting that extrarenal AMPK activation or off-target effects may play a role.

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Figure 1A.

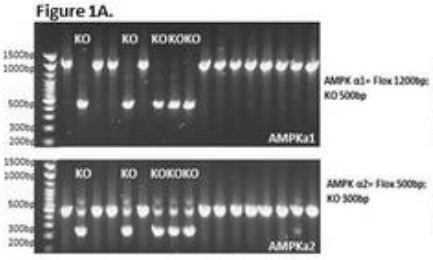


Figure 1B.

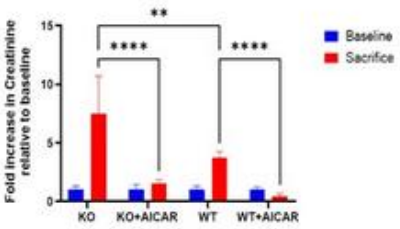


Figure 1C.

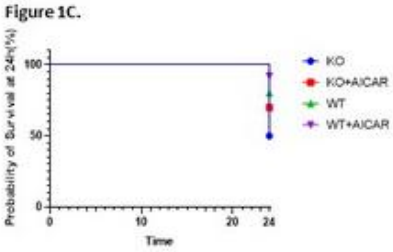
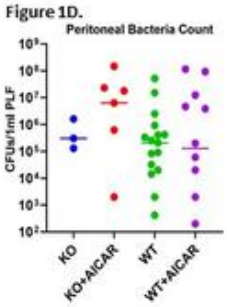


Figure 1D.



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Olfactomedin4 as a Novel Loop of Henle-Specific Acute Kidney Injury Biomarker

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Purpose: Acute kidney injury (AKI) is associated with significant morbidity and mortality. Urinary biomarkers hold the potential to disentangle the clinical heterogeneity and understand pathophysiology of AKI. Olfactomedin4 (OLFM4) is a secreted glycoprotein expressed in mature neutrophils and epithelial cells following stress. In wild type animals with sepsis, OLFM4 expression localized to the kidney, and only to the loop of Henle (LOH). OLFM4 null murine pups with sepsis had higher renal cell apoptosis and higher plasma creatinine. We hypothesized that urine OLFM4 (uOLFM4) will be increased in children with AKI and sepsis.

Methods: Urine from day 1 of admission was obtained from a single center retrospective repository. Samples were chosen based on AKI and sepsis status. Demographic and lab data, including NGAL, were collected from the medical record. uOLFM4 was tested with a custom bead based Luminex immunoassay. AKI was defined by KDIGO stage 2-3 (severe) criteria. Immunofluorescence on biopsy samples from patients with kidney injury was used with antibodies specific for uromodulin and OLFM4.

Results: Eight patients had no sepsis, no AKI; 10 had no sepsis, yes AKI; 10 had sepsis, no AKI; 9 had sepsis and AKI. Children with AKI had increased uOLFM4 compared to no/stage 1 AKI ($p=0.04$). Similarly, children with sepsis had increased uOLFM4 compared to no sepsis ($p=0.04$). There was statistically significant correlation between uOLFM4 and urine NGAL (r2 0.40, $p=<0.0001$), but there are patients with high uOLFM4 and low NGAL and vice versa. The product of NGAL and uOLFM4 didn't increase ability to predict AKI compared to NGAL alone ($p=0.002$ vs $p=0.0018$). Immunofluorescence demonstrated OLFM4 signal colocalized with uromodulin, suggesting OLFM4 localized to the LOH in humans.

Conclusion: AKI and sepsis are associated with increased uOLFM4. There was a correlation between OLFM4 and NGAL, but the product of the 2 doesn't improve AKI prediction. Given OLFM4 colocalization to human LOH, we propose OLFM4 may be a novel LOH-specific AKI biomarker.

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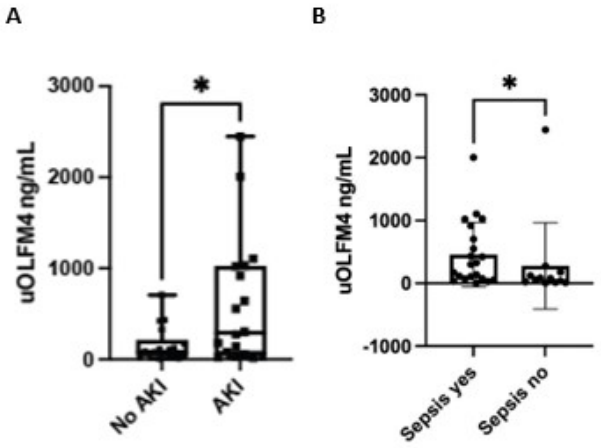

Figure. Urine Olfactomedin 4 levels based on A. AKI status (n=18/group) and B. sepsis status (21 vs 12/group). No-AKI group includes stage 1 AKI.
* Denotes p <0.05. uOLFM4-urine olfactomedin4.

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Urinary Biomarkers as Predictors of AKI in COVID-19 Hospitalized Patients with Pneumonia

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Introduction:The COVID-19 disease manifests in most cases as a lower respiratory tract infection. COVID-19 enters the human body using angiotensin-converting enzyme 2, this could be significant in many ways:AKI, proteinuria, and/or microhematuria could be associated with penetration of the virus into cells.The use of microalbuminuria as a marker for AKI was shown in an animal model and correlated with other markers. .NGAL has been tested in multiple studies of patients at risk of AKI due to sepsis, cardiac surgery, exposure to contrast media, or after kidney transplantation.The most frequently reported causes of admission to the intensive care unit in patients with COVID-19 are hypoxemic respiratory failure that requires invasive mechanical ventilation or hypotension that requires support with vasoactive amines.

Methods:A prospective observational study. Patients who came to the area for COVID-19 were recruited. Upon admission, a urine sample was analyzed with Getein 1100, by quantitative immunofluorescence to determine levels of microalbuminuria and NGAL in 50 patients with creatinine <1.0. All patients had high oxygen requirements (> 5 liters/minute). All patients who had a positive PCR test for SARS CoV-2 were included and patients with a history of chronic kidney disease, urinary symptoms, underlying urological disease or complications of Diabetes or hypertension were excluded. Laboratories were collected at admission and 5 days after admission to compare with initial Ngal and microalbuminuria levels.

Results:The association of the variables was analyzed using the Spearman correlation coefficient, since they are continuous variables. It was found that an elevation of creatinine at day 5 and an initial Ngal> 200 and microalbuminuria >30 have a moderate correlation (rho = 0.46) with a p <0.05, and a low correlation (rho = 0.28) and a p <0.05, respectively.

Conclusion:Although there is no ideal biomarker for acute kidney injury, current biomarkers can significantly predict the development of acute kidney injury, especially in critically ill patients. With the emergence of COVID-19 disease, it is necessary to be able to prevent and treat acute kidney injury on time, in order to reduce the morbidity and mortality of these patients. In this study, it is observed that 2 biomarkers have a significant correlation to predict acute kidney injury, and it is necessary to have more availability of these biomarkers to detect it on time

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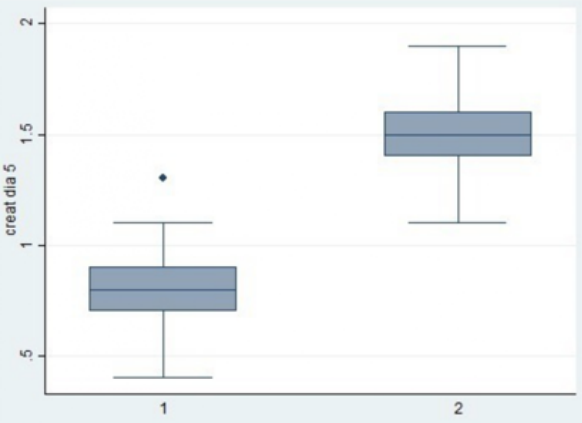

Fig1. Correlation of Ngal >200 and creatinine leves at day 5.

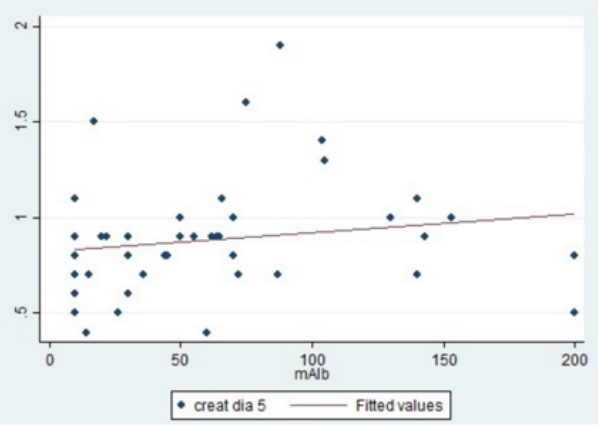

Fig2. Correlation of mAlb leves and creatinine at day 5.

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TAKING FOCUS 2: Using a Clinical Decision Algorithm to Risk Stratify and Manage Critically Ill Pediatric Patients at Risk for Acute Kidney Injury

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Children admitted to the pediatric ICU (PICU) are at risk of developing acute kidney injury (AKI). Identifying those at highest risk is valuable as it may help mitigate its associated poor outcomes. The Renal Angina Index (RAI) has been validated to predict PICU patients (pts) most likely to have severe AKI (KDIGO stage ≥2) 72 hours after PICU admission, and its performance is enhanced by the urinary biomarker neutrophil gelatinase-associated lipocalin (NGAL). We combined these tests with a standardized furosemide stress test (FST) to develop a clinical decision algorithm (CDA) used in the PICU to risk stratify patients for severe AKI.

The CDA (Figure 1) was utilized prospectively for all pts admitted to the PICU beginning in 07/2018 as part of TAKING FOCUS 2 (NCT03541785). An automated RAI was calculated for all pts by the electronic health record (EHR) 12 hours after admission, and a conditional NGAL order released for RAI≥8 (RAI+). A standardized FST was performed in pts with NGAL≥150ng/ml (NGAL+) or in those who were anuric. Response to FST was defined as urine output ≥3mL/kg/hr in either 2 or 6hrs after dosing, or 200mL in the 2hrs after for pts ≥70kg (FST-R); non-responders (FST-NR) failed to meet these thresholds. Outcomes of interest were the presence of severe AKI on PICU days 2-4 and renal replacement therapy (RRT) use. Pts who were RAI+/NGAL+ and FST-NR were predicted to have both outcomes.

1772 patients entered the CDA. 351 (20%) were RAI+, and 262 (75%) had NGAL appropriately sent, a median of 3.1hr (IQR 0.95, 6.85) after the RAI. 158 of 351 (57%) RAI+ pts were NGAL+ or anuric. 46 (29%) of RAI+/NGAL+ pts underwent FST, an average of 21.9hr (SD 19.8) after the RAI resulted, and 16 (35%) were FST-NR. Severe AKI was more common in RAI+ vs. RAI- pts (45 vs. 1.8%, $p<0.001$; 98% NPV). Adding NGAL+ (RAI+NGAL+) increased PPV for severe AKI from 45% to 69%, and RAI+NGAL+ pts had significantly higher rates of severe AKI compared to all others (68 vs. 3.7%, $p<0.001$). Though severe AKI rates did not differ significantly between FST-R (47.6%) and FST-NR (71.4%, $p=0.4$), FST-NR had higher incidence of RRT use (44 vs. 10%, $p=0.02$).

We have successfully operationalized an EHR-embedded CDA that provides timely information about severe AKI risk to bedside providers. Use of the CDA reliably rules out pts at low risk for severe AKI, and identifies those at highest risk who may benefit from earlier, proactive management, including provision of RRT.

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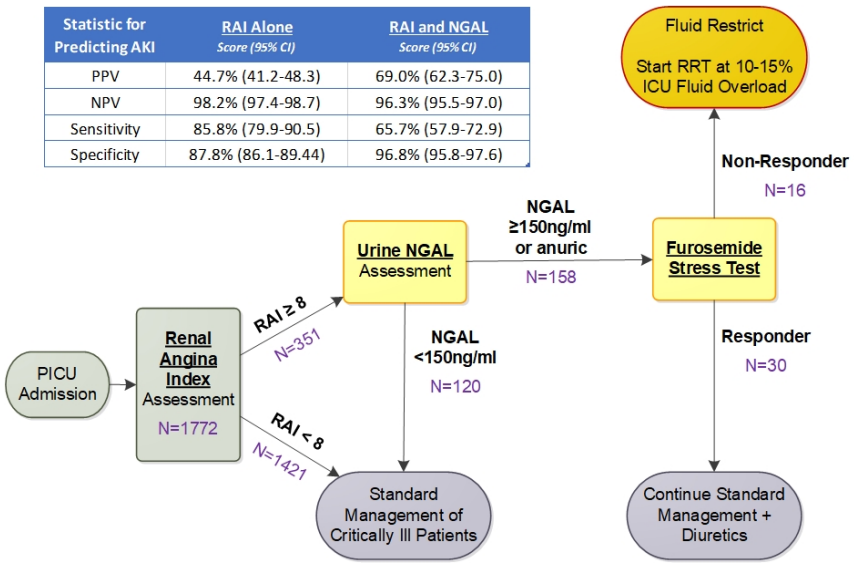
Statistic for Predicting AKI	RAI Alone *Score (95% CI)*	RAI and NGAL *Score (95% CI)*
PPV	44.7% (41.2-48.3)	69.0% (62.3-75.0)
NPV	98.2% (97.4-98.7)	96.3% (95.5-97.0)
Sensitivity	85.8% (79.9-90.5)	65.7% (57.9-72.9)
Specificity	87.8% (86.1-89.44)	96.8% (95.8-97.6)



Abstract Category: B) Research in AKI

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Administration of Mesenchymal Stromal Cell-derived Exosomes is an Effective Rescue Therapy for Progressive Acute Kidney Injury in Rats

Christof Westenfelder[1], Anna M Gooch[1]

[1]*University of Utah*

Background: Preclinical and clinical studies have shown Mesenchymal Stromal Cells (MSCs) to be effective for prevention of AKI [NCT00733876]. Yet studies where MSCs are given 48 hrs. post-insult, a time at which most patients with severe AKI are diagnosed and when no rescue therapy is available, show them to be ineffective or even damaging due to compromised renal blood flow in capillary beds, where introduction of large cells has the potential to cause further deterioration of renal function [NCT01602328]. While MSCs' renoprotection is largely due to their release of beneficial cytokines and exosomes, their potential negative impact on renal blood flow is a concern. Administration of MSC-derived exosomes is known to exert beneficial effects that are similar to those of the parent cells. We hypothesized that since MSC-derived exosomes can prevent AKI, their small size and ability to move through the compromised microvasculature might allow them to also be an effective rescue therapy for late stage AKI where MSCs are ineffective.

Methods: MSCs from Sprague Dawley (SD) rats were used. Their purified exosomes were characterized for size by nanoparticle tracking analysis, protein concentration, gene expression of relevant markers, FACS (CD44 and CD29), and rtPCR. I/R AKI (50-52 min bilateral renal pedicle clamp) was induced in 3 groups of SD rats (6-8/group). SCr was assessed at baseline, Days (D) 1 and 2. If the SCr value on D2 was greater than that on D1, then on D3, rats were given via the suprarenal aorta either 1 ml of Vehicle, 4x10e10 exosomes, or 2x10e6 MSCs. Studied Endpoints: SCr at Days 0-9; survival and renal injury.

Results: In contrast to what is found when MSCs are administered to rats immediately upon reflow, when administered to rats 48 hrs post-I/R AKI, 2x10e6 MSCs prove ineffective at ameliorating injury, while MSC-derived exosomes significantly and sustainably improve renal function by D5 postinjury.

Conclusion: MSC-derived exosome therapy administered 2 days post-insult, when renal blood flow is compromised, but also when most clinical instances of AKI are diagnosed, is superior to MSC therapy for rescue of AKI, likely due to the mirrored paracrine content, but significantly smaller size of exosomes compared to MSCs. Our results support the hypothesis that MSC-derived exosomes could be used as a rescue therapy for non-spontaneously recovering and progressive AKI.

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Urine Biomarkers of Acute Kidney Injury in Extremely Low Gestational Age Neonates. A Nested Case Control Study of 21 Candidate Urine Biomarkers.

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Introduction
Whether biomarkers can be used to diagnose AKI during the first postnatal week in premature neonates has yet to be determined. As the normative values of many urine biomarkers in premature babies vary significantly by gestational age, postnatal age, and gender, these parameters need to be carefully controlled when performing comparison studies.

Methods
We performed a nested case-control study of 20 ELGANSs with severe AKI (state 2 or higher by KDIGO SCr criteria), and 40 controls. We matched cases (1:2) to controls for the same GA week (rounded down to the nearest week), gender, and birthweight (+/- 50 g), Urine was collected at the following pre-determined postnatal timepoints: Day 1 (days 0-3), day 5 (days 4-6) and day 8 (days 7-9). Samples were run in duplicate. To determine the difference in urine biomarker value between groups we used linear mixed model with random intercept for match and random effects across day within cases and matching controls.

Results:
Cases included 8 male and 12 females; GA (24 week = 5; 25 week = 9; 26 week = 4; 27 week = 2); mean (sd) birthweight = 714.5 (187) grams. The group demographic characterisitcs did not differ significantly. The effect size (the mean log10 difference between cases and control pairs) were statistically significantly higher in cases than controls for Cystatin c on day 9 (0.62 (0.12, 1.12); p=0.01), fibroblast growth factor (FGF) 23 on day 8 (0.50 (0.18, 0.83); p = 0.002) Gherlin on day 5 (0.57 (0.09, 1.04); p=0.02), Interleukin (Il) -15 on day 8 (0.43 (0.07, 0.79); p=0.01), kidney injury molecule (KIM)-1 on day 8 (0.34 (0.01, 0.67); p=0.05 and vascular endothelial growth factor (VEGF)a on day 5 (0.45 (0.11, 0.79); p=0.001). Alternatively, the mean differences were statistically significantly lower for cases than controls for: epithelial growth factor (EGF) on day 1 (-0.17 (-0.32, -0.03); p<0.02, IL-15 on day 1 (-0.25 (-0.46, -0.05); p< 0.02), uromodulin (UMOD) on day 1 (mean difference = -0.24 (-0.41, -0.06); p<0.01.

Conclusions
In this nested matched case-control study of ELGANs we show that urine cystatin C, FGF 23, Gherlin, IL-15, KIM-1, VEGFa, EGF, UMOD differ in those with severe AKI vs. no AKI during the first postnatal week.

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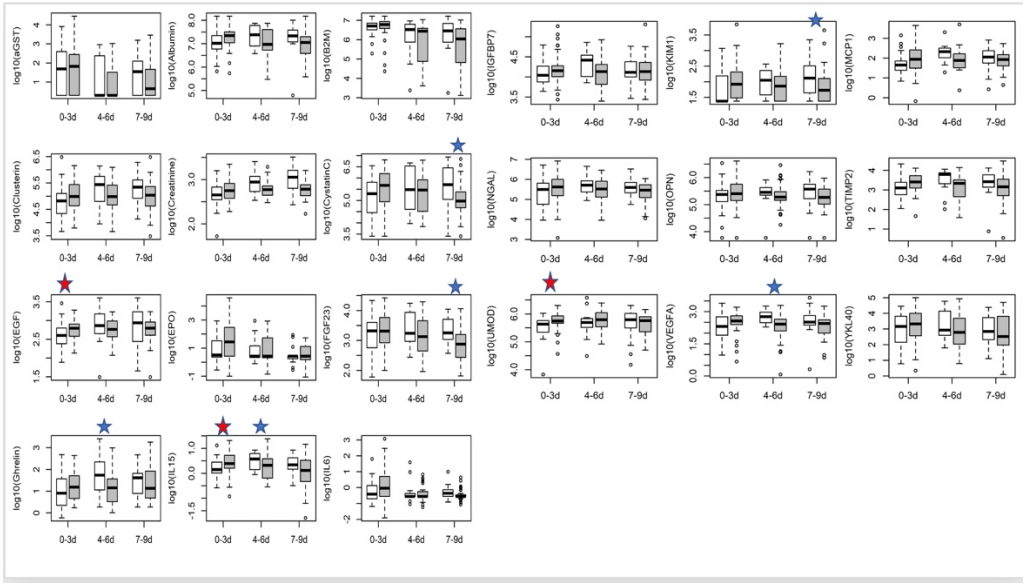

Abstract Category: B) Research in AKI

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Human Amnion Epithelial Cells and Their-derived Exosomes Alleviate Sepsis-associated Acute Kidney Injury via Regulating Endothelial Dysfunction

Dongxuan Chi[1], Ying Chen[2], Chengang Xiang[2], Hui Wang[3], Damin Xu[2], Nan Li[1], Suxia Wang[3], Gang Liu[2], Shuangling Li[1], Li Yang[2]

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Background:
Sepsis is characterized by organ dysfunction resulting from a patient's dysregulated response to infection. Sepsis-associated acute kidney injury (S-AKI) is the most frequent complication contributing to the morbidity and mortality of sepsis. The prevention and treatment of S-AKI remains a significant challenge worldwide. In recent years, human amnion epithelial cells (hAECs) have drawn much attention in regenerative medicine, yet the therapeutic efficiency of hAECs in S-AKI has not been evaluated.

Methods:
Septic mice were induced by cecal ligation and puncture (CLP) operation. hAECs and their derived exosomes (EXOs) were injected into the mice via tail vein right after the CLP surgery. The 7-day survival rate was observed. Serum creatinine level was measured and HE staining of tissue sections was performed 16 hours after CLP. Transmission electron microscopy was used to examine the renal endothelial integrity in CLP mice. Human umbilical vein endothelial cells (HUVECs) were treated with lipopolysaccharide (LPS) and EXOs. ZO-1 localization was observed by immunofluorescence staining. Expression of p-p65, p65, VCAM-1 and ZO-1 in the kidney was determined by Western blot.

Results:
hAECs decreased the mortality of CLP mice, ameliorated septic injury in the kidney and improved kidney function. More precisely, hAECs suppressed systemic inflammation and maintained the renal endothelial integrity in septic animals. EXOs from hAECs exhibited similar renal protective effects as their parental cells. EXOs maintained endothelial cell adhesion junction in vitro and inhibited endothelial cell hyperactivation in vivo. Mechanistically, EXOs suppressed pro-inflammatory NF-κB pathway activation in LPS-treated HUVECs and in CLP mice kidneys.

Conclusions:
Our results indicate that hAECs and their derived exosomes may ameliorate S-AKI via the prevention of endothelial dysfunction in the early stage of sepsis in mice. Stem cell or exosome-based therapy targeting endothelial disorders may be a promising alternative for treatment of S-AKI.

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Piperacillin/Tazobactam-Associated Acute Kidney Injury is Associated with Higher Piperacillin Concentration Exposures

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[1]*Cincinnati Children's Hospital Medical Center*

Purpose of the Study: Critically ill patients are at risk for antibiotic toxicity due to changes in drug pharmacokinetics (PK). Piperacillin/tazobactam (PTZ), a commonly used antibiotic, is associated with acute kidney injury (AKI) and is an ideal candidate for precision dosing. The relationship between piperacillin (PIP) concentrations and AKI remains unknown. We estimated PIP exposures in critically ill patients given PTZ to identify PIP concentrations associated with increased risk of piperacillin-associated AKI (PTZ-AKI).

Methods Used: We used an existing dataset of 149 critically ill patients admitted to one PICU, who received 1+ PTZ doses and had 1+ PIP concentrations measured by HPLC. Exclusion criteria were receipt of PTZ for <24 hours, no free PIP concentrations measured, initial PTZ given at another institution, or receiving CKRT, ECMO, or MARS™ therapy. PIP area under the curve (AUC), highest peak (Cmax) and highest trough (Cmin) in the first 24 hours of PTZ therapy were estimated using MWPharm++ (Mediware, Czech Republic), Bayesian estimation, a PIP population PK model, and patient concentrations. PTZ-AKI was determined by 3 physician adjudicators based on: 1) AKI present for >24 hours after exposure to the first PTZ dose, 2) AKI met KDIGO stage 2 or 3 criteria and 3) increase in serum creatinine (SCr) >0.5 mg/dL when baseline SCr was below 0.5 mg/dL. Adjudicators rated the likelihood of PTZ-AKI using the Naranjo Adverse Drug Reaction Probability Scale. T-test of log-transformed PIP concentration measurements (AUC, Cmax, Cmin) was used to analyze differences between groups.

Summary of the Results: 107/149 patients were included. Adjudicator consensus on PTZ-AKI presence was 82%; 16 patients (15%) met all 3 criteria and were rated as possibly or probably having PTZ-AKI. Patients with PTZ-AKI weighed more (44.7 vs. 17.7 kg, $p<0.001$). AUC and highest Cmin in the first 24 hours were higher in patients with PTZ-AKI (2042 vs. 1445 mg*hr/L, $p=0.03$; 50.1 vs. 10.7 mg/L, $p<0.001$; Fig 1).

Conclusion reached: We used a robust adjudication process to determine PTZ-AKI and show a relationship between PIP AUC and highest Cmin in the first 24 hours of PTZ therapy and development of PTZ-AKI, signifying that total exposure to piperacillin early in the PTZ course is associated with AKI development. These data could serve as the foundation for implementation of therapeutic drug monitoring and precision dosing to reduce AKI incidence in patients treated with PTZ.

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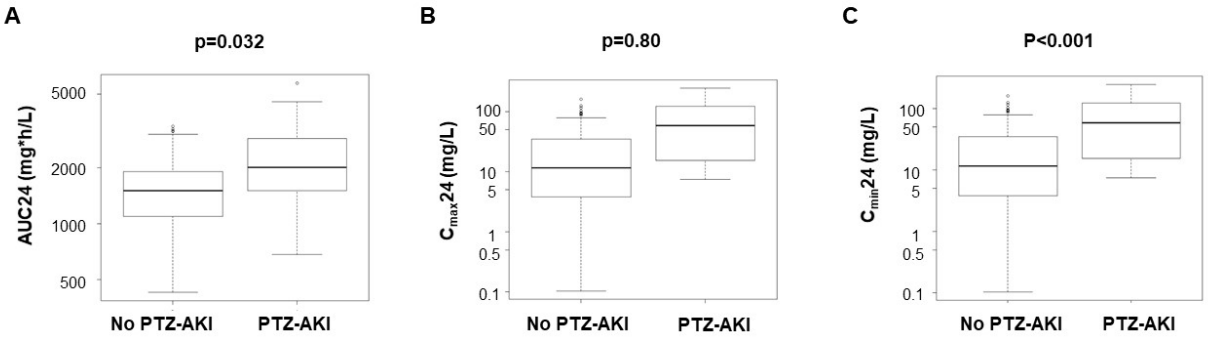
Figure 1: Box plots, with y-axes on the log scale, comparing (A) area under the curve (AUC) in the first 24 hours of PTZ exposure, (B) highest peak (C_{max}) in the first 24 hours, (C) highest trough (C_{min}) in the first 24 hours between patients without and with piperacillin/tazobactam-associated AKI (PTZ-AKI).
Dark line = median, upper and lower limits of box = interquartile range



Abstract Category: B) Research in AKI

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Histological Patterns Of Post Covid Acute Kidney Injury (AKI):A Myriad Of Presentations

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Purpose of the Study :
Covid – 19 is relatively a new disease with varied presentations which can affect multiple organs including kidney. AKI is quite commonly associated with covid-19 infection. However, very little is known about the pathophysiology associated. Our study aims at finding about the variety of pathologic mechanisms and histologic aspects involved in covid 19 associated AKI. The results are obtained from biopsy specimens.

Materials and methods :Patients with a history of covid – 19 developing AKI have been identified. AKI was diagnosed by Kidney Disease Improving Global Outcomes (KDIGO) criteria. Patients were subjected to renal biopsy. A retrospective analysis of biopsies of 45 patients was done. The data has been collected from multiple centers of the Telangana State, India.

Results : Patient's age varied from 2 to 76 years. Among all the patients, 36 are male, 9are female.The duration between Covid infection and AKI ranged from 2 weeks to 6 months. 11 patients showed ATIN (24.4%),11 patients showed acute tubular injury (24.4%) , 3 patients showed crescentic glomerulonephritis (6.6%), 3 patients showed changes suspicious of TMA(6.6%),2 patients showed collapsing glomerulopathy(4.4%),3 patients showed oxalate deposition in tubules (6.6%),3 showed changes of IRGN (6.6%), rest,i.e,9 (20%) showed changes of background disease.

Conclusion:AKI followed by covid 19 has a variety of pathologic mechanisms .Studying the patterns and their further follow up will be beneficial since there is very limited data.

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Pediatric Kidney Transplantation as a Potential Clinical Model of Acute Kidney Injury

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Background: Ischemia-reperfusion injury (IRI) is a mechanism of acute kidney injury (AKI). Similar to cardiopulmonary bypass, kidney transplantation can be thought of as controlled IRI, which results in acute tubular necrosis and may lead to delayed graft function (DGF). Therefore, we sought to investigate kidney transplantation in a pediatric population as a clinical model of AKI and identify predictors of DGF.

Methods: This is a retrospective and prospective observational cohort study of patients aged 3 months to 26 years who underwent kidney transplantation at Cincinnati Children's Hospital Medical Center between 11/1/2017 and 11/30/2021 with prospective enrollment starting 7/1/2020. Prospective patients had urine specimens collected for future urine biomarker testing. Delayed graft function (DGF) was defined as receiving kidney replacement therapy (hemodialysis or continuous kidney replacement therapy) within 7 days post-transplant. Categorical data were analyzed using Fisher's Exact test and continuous data were analyzed using Wilcoxon rank sum test with significance <0.05. Multivariable analysis was completed with univariate predictors with p value <0.2 and of clinical significance.

Results: 10/90 (11%) patients developed DGF. There was no difference in sex, race, age at transplant, etiology of kidney disease, pre-transplant dialysis, pre-transplant calculated panel reactive antibody (cPRA) level, organ donor type, human leukocyte antigen (HLA) mismatch, kidney donor profile index (KDPI) or lymphocyte-depleting induction immunosuppression. Patients with DGF had longer warm ischemia times (51 vs 37 minutes, $p=0.0009$) with no difference in total and cold ischemia time. Patients with DGF who received deceased donor kidneys were less likely receive machine perfusion prior to transplant. Multivariable analysis of the total cohort revealed that there were no independent predictors of DGF, but warm ischemia time did trend toward significance ($p=0.054$).

Conclusion: The 11% of patients who developed DGF were found to have longer warm ischemia times in the total cohort. Those with DGF were less likely to have received machine perfusion prior to deceased donor transplant in the total cohort. The next steps will include analysis of urinary biomarker in the prospective cohort to evaluate IRI during pediatric kidney transplantation as a model of AKI.

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Table 1: Analysis of Patients with and without Delayed Graft Function

	Delayed Graft Function (n=10)	**No Delayed Graft Function (n=80)**	***Univariate P Value***	***Multivariable P Value***
Demographics				
Male	5 (50%)	47 (59%)	*0.74*	
African American	2 (20%)	9 (11%)	*0.35*	
Age at Transplant (y)*	14.3 (9.6 – 17.3)	11.5 (4.1 – 16.3)	*0.18*	*0.88*
Primary Glomerular Diagnosis	5 (50%)	26 (33%)	*0.30*	
Prior Kidney Transplant	0	6 (8%)	*1*	
Pre-Transplant Dialysis	9 (90%)	59 (74%)	*0.44*	
Pre-Transplant cPRA (%)*	0 (0 – 0)	0 (0 – 1.3)	*0.48*	
Deceased Donor Organ	8 (80%)	41 (51%)	*0.10*	
Machine Perfusion	0 (0%)	18 (44%)	***0.02***	*0.99*
KDPI (%)*	20 (10.8 – 26)	11 (5-20)	*0.14*	*0.33*
HLA Mismatch				
Total*	4 (3.3-4.8)	3 (2-5)	*0.52*	
0 MM 1-5 MM 6 MM	0 10 0	1 77 2	*1*	
Ischemia Time*				
Cold Ischemia	442.5 (350.8 – 670.5)	271 (41.3 – 788)	*0.15*	*0.59*
Warm Ischemia	51 (45 – 56.8)	37 (30 – 43)	***0.0009***	*0.054*
Total Ischemia	497 (397.5 – 738.5)	305.5 (80.3 – 827)	*0.13*	
T-Cell Depleting Induction	2 (20%)	14 (18%)	*1*	

*(median, IQR)

Abstract Category: B) Research in AKI

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Extracellular Vesicles Derived from Endothelial Progenitor Cells Protect Human Glomerular Endothelial Cells and Podocytes from Complement- and Cytokine-Mediated Injury

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Background: Glomerulonephritis (GN) are still responsible for 5-10% of AKI cases during hospitalization. Glomerular endothelial cells (GEC) and podocytes (Podo) are the main targets of inflammatory reaction potentially leading to the progression toward chronic kidney disease (CKD). Activation of the complement cascade (Compl) and pro-inflammatory cytokines (CK) such as Tumor Necrosis Factor-α (TNF-α) and Interleukin-6 (IL-6) can alter GEC and Podo function during GN. Endothelial Progenitor Cells (EPC) are bone-marrow-derived hematopoietic stem cells able to repair injured endothelium by releasing paracrine mediators such as Extracellular Vesicles (EV), microparticles involved in intercellular communication by transferring proteins and RNAs to target cells.

Study aim: to evaluate in vitro the protective effect of EPC-derived EV on GEC and Podo cultured in detrimental conditions with inflammatory CK (TNF-α/IL-6) and the Compl protein C5a.

Methods: GEC and Podo were isolated from human glomeruli and cultured in detrimental conditions (C5a and CK) mimicking GN in different experimental procedures. EPC were isolated from peripheral blood of healthy volunteers and characterized for endothelial and stem cell markers. EVs were isolated from EPC supernatants by ultracentrifugation and characterized for size/concentration (Nanosight), protein (FACS) and RNA (microarray) expression.

Results: EVs were internalized in GECs and Podo through a L-selectin-dependent mechanism. In GEC, EV enhanced the formation of capillary-like structures and cell migration by modulating gene expression and inducing the release of growth factors (VEGF-A and HGF). In the presence of CK and C5a, EPC-derived EVs protected GEC from apoptosis by decreasing oxidative stress and prevented leukocyte adhesion by inhibiting the expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin). On Podo, EV inhibited apoptosis and prevented nephrin shedding induced by CK and C5a. In a co-culture model of GEC/Podo that mimicked glomerular filtration barrier, EPC-derived EV preserved cell function and permeselectivity from inflammatory-mediated damage. RNase pre-treatment of EV abrogated their protective effects, suggesting the crucial role of RNA transfer from EV to damaged glomerular cells.

Conclusion: EPC-derived EV preserved GEC and Podo function from complement- and cytokine-induced damage, suggesting their potential role as therapeutic agents for AKI due to drug-resistant glomerulonephritis.

Abstract Category: B) Research in AKI

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Renal Functional Reserve and Serum Creatinine Increase After Nephrectomy For Living Donor Kidney Transplantation: Is It Really AKI?

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Background: Living Donor Kidney Transplantation represents nowadays the best therapeutic option for end stage kidney disease patients. After nephrectomy, living kidney donors (LKD) develop a partial loss of renal function (RF) that can be defined as AKI according to KDIGO criteria: clinical consequences of this AKI episode on long term RF have not been yet investigated. Recovery from AKI is due to the presence of renal functional reserve (RFR), defined as the capacity of the kidney to increase GFR.

Study aim was to analyze RF in LKD at different time points in both a static (estimated and radioisotopic GFR) and a dynamic (RFR) manner integrated with urinary levels of AKI biomarkers (NGAL, Nephrocheck) to detect a possibile CKD progression.

Methods: 50 LKD were enrolled and RF was studied at different time points by serum creatinine (sCr) and using radioisotope GFR with 51Cr-EDTA with a concomitant sequential functional scintigraphy with 99mTc-MAG to determine split renal function. RFR was assessed by oral protein load following Vicenza's protocol. Urinary biomarkers of tubular injury (NGAL, Nephrocheck) were also evaluated.

Results: LKD median age was 55, sCr 0.70 mg/dL, eGFR (CKD-EPI) 101 mL/min, radioisotopic GFR 98 mL/min. Mean % of renal function of the right kidney was 47.4 ml/min. Immediately after nephrectomy, all LKD worsened renal function with a median sCr of 1.2 mg/dL (1.1-1.4): 7 days after surgery, renal recovery was observed in all cases and median sCr was significantly lower 1.04 mg/dL (0.9-1.3) than at the zenith. Urinary NGAL and Nephrocheck were negative in all LKD. One year after nephrectomy, median radioisotopic GFR was 64 mL/min (44-87) vs. 46 mL/min (38-65) before donation with an average compensatory GFR increase of 18 mL/min (0.8-46). A linear correlation between pre-donation RFR and the compensatory GFR increase was found (r=0.66). Of interest, 1 year after donation, LKD maintain a certain amount of RFR and all LKD showed normal levels of urinary injury biomarkers.

Conclusion: Post-donation AKI is a functional state probably not correlated with a structural tissue damage as suggested by the negative values of urinary biomarkers, thus with a low risk of CKD progression. RFR provides a dynamic and prognostic evaluation of RF in LKD allowing an increase of donor numbers even in presence of some comorbidities. Moreover, RFR can be used to estimate GFR increase post-donation, providing more accurate information on RF of LKD.

Abstract Category: B) Research in AKI

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Aristolochic Acid-Induced Nephropathy Is Attenuated In Mice Lacking The Neutral Amino Acid Transporter B0AT1 (SLC6A19)

Aleix Navarro Garrido[1], Young Chul Kim[1], Helen Goodluck[1], Sadhana Kanoo[1], Maria Crespo-Masip[1], Yuji Oe[1], Stefan Bröer[2], Volker Vallon[1]

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Background: B0AT1 (Slc6a19) mediates the absorption of neutral amino acids, including branched-chain amino acids (BCAA), in the intestine as well as kidney, where it is expressed in early and mid-proximal tubule (S1/S2). Dietary restriction of BCAA has been proposed to improve metabolic health by inhibiting mTOR and inducing autophagy. Here we determined how gene-targeting of Slc6a19 in mice affects basal kidney function and the nephropathy induced by aristolochic acid (AA), which targets the proximal tubule.

Methods: Littermate female B0AT1-deficient (Slc6a19-/-), heterozygote (Slc6a19+/-) and wild-type (WT) mice were given AA (10 mg/kg i.p.) or vehicle every 3 days for 3 weeks, and analyses performed after the last injection ("active phase") or 3 weeks later, when mice were euthanized and kidneys, hearts and livers harvested for RTqPCR and fibrosis analyses ("recovery phase").

Results: Vehicle-treated Slc6a19-/- mice lacked renal mRNA expression of B0AT1, associated with lesser expression of the related amino acid transporter B0AT3 (Slc6a18) vs. WT. This may in part be due to KO model generation, as B0AT1 and B0AT3 are co-expressed side-by-side on the same chromosome. Urinary albumin/creatinine ratio (UACR) was modestly higher in vehicle-treated Slc6a19-/- mice, associated with lesser renal megalin mRNA expression. AA reduced body and kidney weight and hematocrit, and increased plasma creatinine (as an indicator of reduced GFR) largely independent of genotype. Absence of B0AT1, however, prevented the increase in UACR and attenuated the renal upregulation of pro-inflammatory markers Ccl2 and Ccr2 and pro-fibrotic markers Timp1, Tgf-β1, and Col1a1 in response to AA. In accordance, AA-induced fibrosis, measured by Masson's trichrome staining, was attenuated in mice lacking B0AT1.

Conclusions: Genetic deletion of B0AT1 modestly impairs basal proximal tubule function including the reuptake of albumin. On the other hand, absence of B0AT1 prevented AA-induced increase in UACR and attenuated the associated renal inflammation and fibrosis, suggesting a potential protective effect of B0AT1 inhibition in response to AA-induced nephropathy.

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Reduction of Intraoperative Nephrotoxic Antimicrobial Exposure Can Improve Renal Recovery in Patients undergoing Heart Transplantation.

Syed Quadri[1], Jonathan Kelly[1], Caroline Perez[1], David Taber[1], Ryan J Tedford[1], Shayma Alzaidi[1], Holly B Meadows[1], Blaithin A McMahon[1]

[1]*Medical University of South Carolina*

Purpose: The purpose of this study was to evaluate the impact of reducing intraoperative nephrotoxic antibiotic exposure on the rate of Acute Kidney Injury and renal recovery in adult patients undergoing heart transplantation.

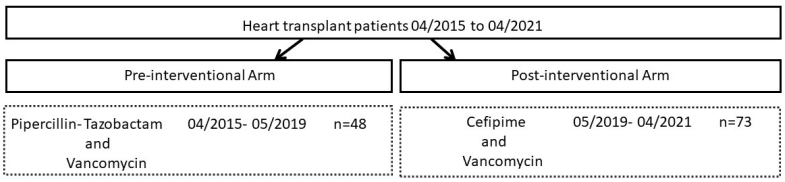
Methods: This is a single-center prospective study design of all adult patients undergoing heart transplants at Medical University of South Carolina between 4/12/2015 to 4/17/2021. In 06/20/2019, we changed empiric intraoperative antimicrobial coverage from piperacillin-tazobactam to cefepime while continuing vancomycin use. We collected data using the electronic health record. AKI severity and recovery were extracted for patients exposed to piperacillin-tazobactam and vancomycin or cefepime and vancomycin. AKI was identified using KDIGO serum creatinine criteria. Renal recovery was defined as 25% improvement in serum creatinine within 7 days. We assessed rates of nephrotoxin exposure and KDIGO AKI rates in all 121 heart transplant inpatients for at least 4 years pre-intervention and 1 year and 9 months post-intervention. Secondary outcomes eGFR at 3 and 6 months, worsening CKD or diagnosis of ESRD at 6 months, length of ICU and hospital stay, and readmissions within 6 months.

Results: While the rates of all KDIGO stages of AKI remained the same after the intervention, the rates of recovery of AKI prior to hospital discharge improved 7.5-fold in the intervention group (45.0% vs 6.0 %, $P < 0.05$).

Conclusion: Reduction of nephrotoxic antimicrobial exposure can improve AKI recovery rates post heart transplantation.

Methods

Prospective, non-randomized, open-label study



Antibiotic	Mean dose	Median dose
Piperacillin-tazobactam	17.7 G	18 G
Vancomycin	1180 mg	1250 mg

Antibiotic	Mean dose	Median dose
Cefipime	4.0 G	4.0 G
Vancomycin	1250.9 mg	1250 mg

Abstract Category: B) Research in AKI

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Successful Parallel use of CArdio-Renal PEdiatric Dialysis Emergency Machine (CARPEDIEM) and Extracorporeal Membrane Oxygenation (ECMO) for Infant Kidney Support Therapy (KST)

Jolyn Morgan [1], Amanda Snyder [1], Francisco Flores [1], Reanna Smith [1], Alexis Benscoter [1], Cara Slagle [1], Stuart Goldstein [1]

[1]*Cincinnati Children's Hospital Medical Center*

Background: The sensitive access and return pressures (RP) registered by CARPEDIEM (CD) causes concern that CD could be incompatible with the pressures generated by ECMO. We describe an in vitro simulation trial connecting CD to an ECMO circuit using expired red blood cells and translation to a bedside experience.

Methods: In vitro simulation: the 1st approach connected CD bloodlines to the positive pressure portion of ECMO. CD access was attached to the first port post pump head with a c-clamp applied to generate a negative access pressure (AP). CD return was attached to the 2nd port post pump head. As ECMO blood pump flow increased, high pre-membrane pressure (PMP) >200 mmHg triggered CD RP alarms. The microclave was removed from the return port, but alarms persisted. The CD return line was then moved to the venous sampling port (negative flow). A c-clamp was applied to generate a positive RP. The 2nd approach connected CD bloodlines to the negative pressure portion of ECMO. The CD access was attached to the venous bridge port and the return line to the venous sampling port with a c-clamp to generate a positive RP.

Results: We translated lessons learned from in vitro testing to the bedside. A 3.5 kg 6-week infant with congenital diaphragmatic hernia required ECMO and KST for AKI and fluid overload (31%). KST was initially performed via an in-line ECMO hemofilter but inconsistencies between the infusion pump and ultrafiltration led to CD transition. The ECMO blood flow rate (Qb) was 0.52 L/min, venous and PMP were 21 and 216 mmHg, respectively. CVVHD via the CD used a HCD 025 filter, Qb 25 mL/min, and Qd of 4 mL/min. CD bloodlines were connected post pump head but moved pre pump due to high RP (220 mmHg) and PMP (230 mmHg), which is what we saw with in vitro testing. The CD circuit was changed daily, and pressures remained acceptable (mean AP-50; VP 70) for 4 consecutive days. Urea reduction was 64% within 24 hrs. Fluid removal and anticoagulation were managed via ECMO.

Conclusion: We report the first case of CD provision in parallel with ECMO. Successful management of CD pressures was achieved connecting bloodlines pre pump head without altering ECMO Qb. Mitigation of CD alarms allowed uninterrupted therapy and KST dose delivery. Although concomitant use of CD and ECMO does work with our standard connection, we were able to test multiple configurations to bypass high ECMO PMPs.

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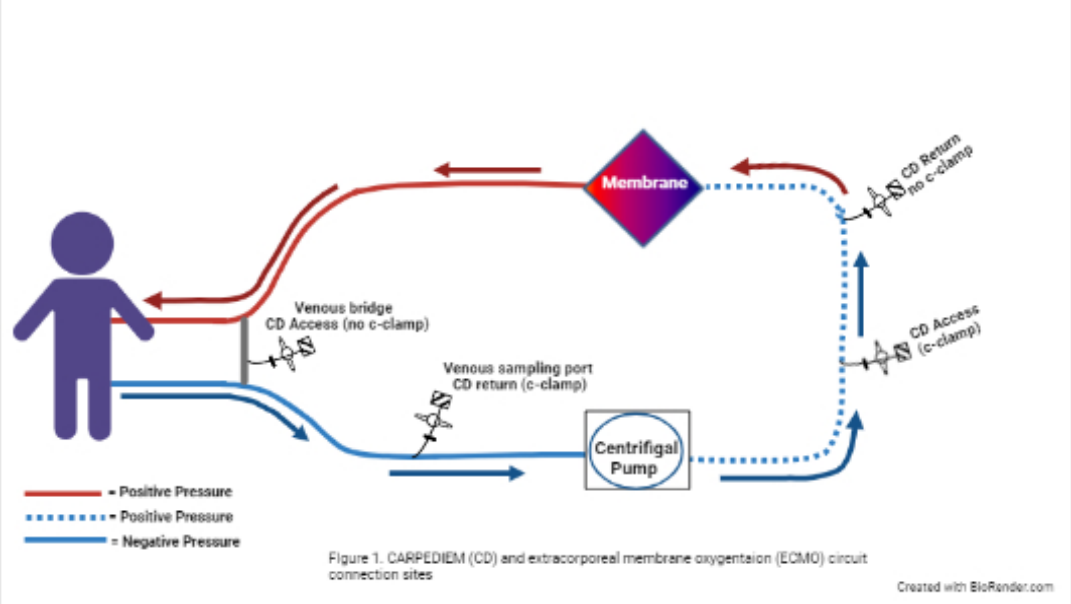

Figure 1. CARPEDIEM (CD) and extracorporeal membrane oxygentaion (ECMO) circuit connection sites

Abstract Category: C) RRT Technique Characteristics

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Circuit to Circuit Blood Priming in Patients Requiring Kidney Support Therapy (KST) with the CArdio-Renal PEdiatric Dialysis Emergency Machine (CARPEDIEM)

Amanda Snyder[1], Jolyn Morgan[1], Stuart Goldstein[1]

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Purpose: The CARPEDIEM (CD) is a dedicated infant dialysis device that offers small extracorporeal circuit volumes (ECV) decreasing the need for blood priming. Although the smallest CD filter available in the US (HCD 015) has an ECV of 32 mL, infants <4 kg may still require a blood prime. To mitigate individual PRBC unit exposure to infants with filter changes, we describe an in vitro simulation trial of circuit-to-circuit blood priming.

Methods: This in vitro trial was initially performed with two CD machines, using two identical CD filters. A second trial was completed using a HCD 015 filter (ECV 32 mL) and a HCD 025 filter (ECV 41 mL). The machines were first primed with PlasmaLyte TM, and subsequently with PRBCs. Following the blood prime of the 1st circuit, subsequent circuits were primed with the blood contained in the preceding circuit. We detail this step-by-step process.

CARPEDIEM (CD1) to CARPEDIEM (CD2): 1) Prime CD2 with PlasmaLyte™, 2) End CD1 treatment, navigate to end screen to begin new therapy, 3) Clamp and disconnect CD1 arterial/ venous lines from patient, 4) Open CD1 blood pump and remove venous line from venous clamp, 5) Connect CD1 arterial line to adapter spike, spike a bag of normal saline, hang above machine, 6) Connect CD1 venous line to a female adapter and connect CD2 arterial line to open end, 7) Connect CD2 venous line to an empty waste bag, 8) Unclamp all lines, 9) Start CD2 blood flow at 30 mL/min to initiate prime, 10) Press “stop” when prime complete, clamp all lines and prepare to initiate

Summary: Blood was successfully transferred from one machine to another without triggering circuit pressure alarms. Opening the blood pump and removing the venous line from the venous clamp negates alarms that occur when two machines have competing pressures. Each procedure was completed in its entirety within 3 minutes. This method has been implemented twice into clinical practice and performed without incident.

Conclusion: Using this technique to circuit prime minimizes the risks associated with blood product exposure and potential sensitization in a patient that may require future transplantation. It also helps to alleviate time off therapy that may result from blood product preparation time. When performing a circuit to circuit prime, considerations include the differences in ECVs.

Abstract Category: C) RRT Technique Characteristics

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Vascular access in infants weighing less than 10 kg

Mariko Sawada[1], Kazutoshi Ueda[1], Kayo Ogino[1], Tomohiro Hayashi[1], Kenji Waki[1]

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Purpose:
The first step in acute blood purification therapy (BPT) is ensuring a stable vascular access (VA); this is in vital in small children. However, there are few reports on VA in infants. We investigated the VA performance of extracorporeal therapies in infants.

Methods:
This was a single-center retrospective study of 42 infants, weighting less than 10 kg, who underwent acute BPT between January 2006 and August 2021; we excluded the patients with concomitant cardiac pulmonary bypass. We collected demographic, clinical, and laboratory data from medical records and retrospectively analyzed.

Results:
Of patients, 23 (54.3%) were male, 21 (45.2%) were female. The age ranged from 0 to 58 months old (median; 1 month old). Body weight ranged from 0.8 to 9.8 kg (median; 3.6 kg). The primary diseases were sepsis (21 patients), autoimmune disease (10), inborn error of metabolism (3); 8 patients had other diseases. The type of BPT performed varied among patients; 18 patients underwent continuous hemodiafiltration, 13 had polymyxin B-immobilized fiber column direct hemoperfusion, and 11 underwent plasma exchange. Urokinase-coated double lumen catheters of varying sizes were used; the catheter size was 6 Fr in 18 infants, 6.5 Fr in 4, 7 Fr in 9, 8 Fr in 4. A smaller central venous catheter (≦5 Fr), not coated in urokinase, was used in patients weighing less than 2 kg. The catheter insertion sites were the femoral vein in 32 patients, right intrajugular vein in 8, and umbilical vein in 2. The catheter tip position was intra/supra vena cava in 36 patients, right atrium in 6. Blood flow rates ranged from 4 to 40 mL/min (median; 20 mL/min); the average blood flow rate per body weight was 5.5 ±3.3 mL/kg/min. Catheter size was significantly related to body weight and blood flow rate (p value <0.05, <0.05, respectively). The anticoagulant used was nafamostat mesilate in 32 patients and heparin in 11. The duration of BPT was 3.5±3.2 days and was not related to catheter size. There was no failure of bleeding out that led to reinsertion or abandonment of blood purification therapy. The 90-day survival rate was 81.0% (34/42 patients); this differed depending on the primary disease.

Conclusion:
Small size, urokinase-coated, central venous catheters (6, 6.5, 7, and 8 Fr) specialized for dialysis were useful in infants weighing less than 10 kg. In those weighing less than 2 kg, much-smaller non-dialytic catheters were available for performing acute BPT.

Abstract Category: C) RRT Technique Characteristics

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A case of hyperbilirubinemia associated with sepsis with a good outcome after bilirubin adsorption therapy

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Introduction
Bile stasis associated with severe bacterial infections can cause acute lung injury and renal failure due to prolonged hyperbilirubinemia. We report a case of acute hepatic failure secondary to septic shock for whom bilirubin adsorption therapy was treated to prevent further organ damage and who had a good outcome.

Case
A 9-year-old boy was diagnosed septic shock due to Pseudomonas aeruginosa during induction of remission after relapse of B-cell precursor acute lymphoblastic leukemia. His Pediatric Logistic Organ Dysfunction 2 score was 24 points and his Pediatric End-stage Liver Disease score was 17 points. He was critically ill and he was predicted poor prognosis in terms of both his life and liver. The patient received ventilatory support, vasopressors, intravenous fluids, steroids, broad-spectrum antimicrobial agents, continuous hemodiafiltration for acute kidney injury, and endotoxin adsorption therapy in an intensive care unit. Although his blood pressure stabilized and his hepatic enzyme levels tended to improve, his biliary system enzymes increased on the fourteenth day of the disease, and he developed marked hyperbilirubinemia with a total bilirubin level of 25.0 mg/dL and direct bilirubin level of 20.0 mg/dL. There was no improvement despite attempts at diuresis with ursodeoxycholic acid; therefore, bilirubin adsorption therapy (blood separation membrane: OP-05D, plasma adsorption membrane: Plasova BRS, blood flow rate: 50 mL/min, plasma separation rate: 30%, plasma therapeutic dose: 4,500 mL/dose, and anticoagulation: 25 mg/hour nafamostat mesylate) was administered on the sixteenth to eighteenth day. Total bilirubin clearance was 64.4%, 51.8%, and 52.5% on the sixteenth, seventeenth, and eighteenth day, respectively. Total bilirubin and direct bilirubin levels improved to 5.7 and 4.2 mg/dL. Since then, bilirubin has normalized and no complications of organ damage have appeared.

Conclusion
Plasma exchange therapy has been used to treat liver failure in children. However, there are concerns about the large amount of active protein components that are discarded, post-transfusion infections due to the large amount of fresh frozen plasma administered, and huge medical costs. We successfully treated with bilirubin adsorption therapy without large amount of fresh frozen plasma and could prevent further organ damage.

Abstract Category: C) RRT Technique Characteristics

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Outcome of Standard versus No post-filter ionized calcium monitoring in regional citrate anticoagulation for continuous kidney replacement therapy, A randomized controlled trial (NPC trial)

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Background: Post-filter ionized calcium (pfCa) in regional citrate anticoagulation (RCA) for continuous kidney replacement therapy (CKRT) was monitored for maximizing filter lifetime. However, standard monitoring to keep pfCa in the target level can cause potential high citrate dose and citrate loading leading to metabolic complications. This study aimed to determine the outcomes of no pfCa monitoring compared with standard pfCa monitoring in terms of filter life span, citrate dose, citrate-related complication, and mortality.

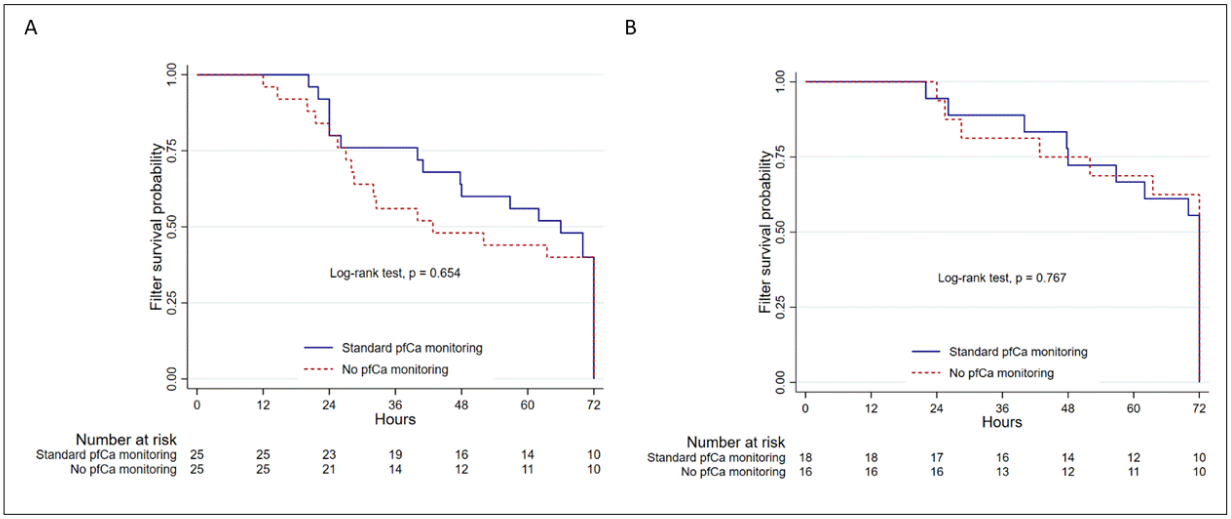
Methods: A non-inferiority randomized trial was conducted between January 2021 to October 2021 at King Chulalongkorn Memorial Hospital. Critically ill patients receiving CKRT with RCA starting citrate dose of 4 mmol/L were randomized to receive either standard pfCa monitoring group, consisted of adjust the citrate dose to achieve pfCa level of 0.25-0.35 mmol/L, or no pfCa monitoring group, consisted of blind the pfCa level and no citrate dose adjustment

Results: Fifty patients were randomized into the standard pfCa monitoring group (n=25) and the no pfCa monitoring group (n=25). The mean filter life span was 54±20 h in the standard pfCa monitoring group vs 47±23 h in the no pfCa monitoring group (95% CI -5.3, 19.5), p=0.25. Compare with the no pfCa monitoring group, the standard pfCa monitoring group had a significantly higher citrate dose (4.43±0.32 vs 4 mmol/L, p<0.001). However, rate of filter clotting, citrate accumulation, citrate overload, hypocalcemia, and mortality were not different between both groups.

Conclusion: Among critically ill patients receiving CKRT with RCA, no pfCa monitoring by prescribing the citrate dose of 4 mmol/L showed non-inferiority to standard pfCa monitoring in terms of filter life span and citrate-related complication. This result suggested that no or less frequent pfCa monitoring was safe and feasible.

Figure on following page

Figure: Kaplan-Meier curves of Filter survival at 72 h



(A) time (h) from continuous kidney replacement therapy with regional citrate anticoagulation initiation until any cause of filter replacement (reach the upper limited time at 72 h following manufacturer's recommendation) or filter termination (filter clotting or non-filter clotting) or citrate discontinuation

(B) time (h) from continuous kidney replacement therapy with regional citrate anticoagulation initiation until filter replacement (reach the upper limited time at 72 h following manufacturer's recommendation) or filter clotting

Abstract Category: C) RRT Technique Characteristics

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Safety of Regional Citrate Anticoagulation (RCA) in Critically Ill Patients with End Stage Kidney Disease (ESKD) on Continuous Kidney Replacement Therapy (CKRT)

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Introduction: Regional Citrate Anticoagulation (RCA) is recommended anticoagulation of choice for continuous kidney replacement therapy (CKRT) in critically ill patients. Multiple studies have emphasized its efficacy in prolonging filter life, and safety for extended periods, when delivered by protocol to achieve targeted metabolic control. However, majority of the studies have been conducted in patients with acute kidney injury. The safety and efficacy of CKRT-RCA in end stage kidney disease (ESKD) has not been extensively reported.

Purpose: The purpose of this audit was to examine the biochemical parameters of ESKD patients admitted in the intensive care unit (ICU) of a single tertiary center who underwent per protocol CKRT-RCA.

Methods: A review of the critically ill patients with ESKD who underwent CKRT-RCA over the past 4 months was done based on the monthly audits. All patients underwent continuous venovenous hemodiafiltration (CVVHDF) with RCA using citrate fluid (citrate 18 mmol/L) administered pre-blood pump to achieve post-filter ionized calcium (iCa) 0.25-0.40 mmol/L. The simplified protocol delivers a fixed effluent volume but variable effluent dose over weight ranges. Calcium gluconate 10% solution was infused to maintain systemic iCa between 1.0-1.15 mmol/L.

Results: Thirteen patients (median age 60) with ESKD were placed on CKRT-RCA after admission to the ICU. Mean APACHE score was 27.9 and 69% of the patients were male. Mean filter life was 33 hours and 32 minutes (uncensored for elective discontinuation). Mean delivered dose was 36 mL/kg/hr. There were no significant issues with sodium, potassium, chloride, magnesium, phosphate or acid-base balance. However, there was a trend towards increasing total calcium levels by 18th hour of the CKRT-RCA. The total to systemic iCa ratio remained less than 2.5 and there were no other markers of citrate toxicity. The total calcium normalized by the 54th hour of the CKRT-RCA. Only serum pH was found to be inversely correlated to the total calcium levels.

Conclusion: CKRT-RCA appeared to be well tolerated in patients with ESKD. The trend towards increasing total calcium was likely related to calcium replacement, changes in serum pH and possibly contributed by imbalances in the mineral and bone metabolism associated with ESKD. Further studies are needed to determine factors that affect calcium metabolism in CKRT-RCA for ESKD.

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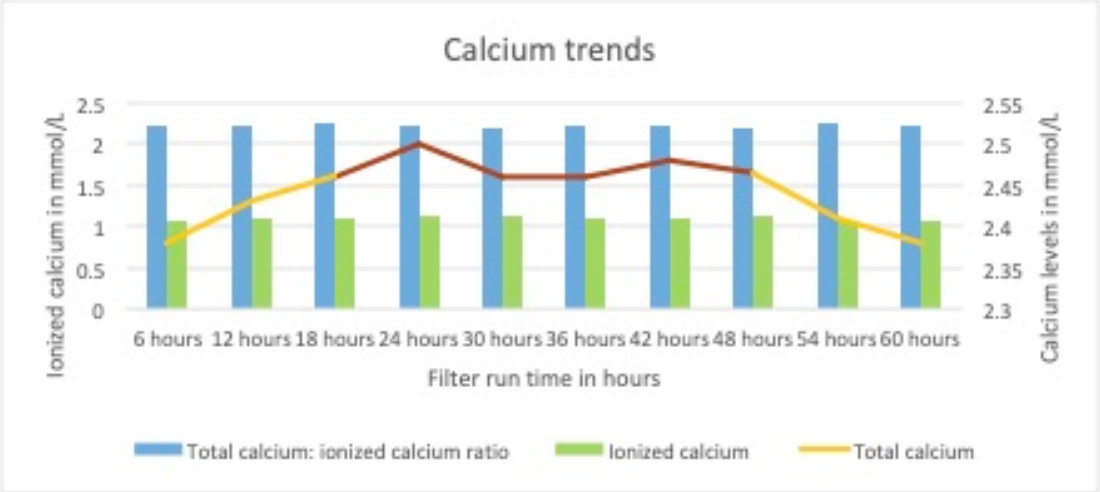

Abstract Category: C) RRT Technique Characteristics

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Retrospective Analysis of Patient and Circuit Complications using Heparin versus Citrate Anticoagulation with Membrane Therapeutic Plasma Exchange in the Pediatric Population

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Background: Data is limited on complications with membrane TPE (mTPE) using heparin anticoagulation and even more sparse data on mTPE using citrate anticoagulation. Membrane TPE with citrate anticoagulation is more challenging than using heparin anticoagulation; however, citrate anticoagulation is beneficial in circumstances in which systemic heparin is considered unsafe.

Objective: We sought to better understand patient and machine complications of mTPE using heparin anticoagulation versus citrate anticoagulation.

Design/Methods: We retrospectively evaluated patients 21 years of age and less who required TPE from 2012 through 2019 at our institution. Patient and machine complications were compared between the patients who received mTPE with heparin anticoagulation versus mTPE with citrate anticoagulation.

Results: Of the 385 procedures evaluated, 5 were excluded because anticoagulation was not used, thus 357 treatments using mTPE with heparin anticoagulation were compared to 23 treatments using mTPE with citrate anticoagulation. Those treated with citrate anticoagulation had a lower first mean ionized calcium (1.12 (1.05-1.18) mmol/L vs 1.25 (1.24-1.27) mmol/L, $p < 0.001$) and more had hypocalcemia (defined as an ionized calcium <1.0 mmol/L) with the first ionized calcium measurement (17.4% vs 5.0%; $p < 0.04$). Subsequent ionized calcium levels did not differ between groups with very rare hypocalcemia in both groups. There were no other significant differences in patient-related complications during treatments including bleeding, fever, hypertension/hypotension, allergic reactions or other. There was no significant difference in machine-related complications between the two groups. Albumin replacement was used more often in the heparin vs citrate treatments (66.4% vs 8.7%; $p<0.001$); while more thawed plasma was used as replacement in the citrate vs heparin treatments (87.0% vs 15.7%; $p<0.001$).

Conclusion: Although we report a small sample size, this study demonstrates that our protocol using mTPE with citrate anticoagulation is not associated with higher rates of machine-related complications. Although the overall rate of hypocalcemia at the first measure of ionized calcium occurred more commonly with citrate anticoagulation treatments, with adjustment of calcium infusion, sustained hypocalcemia was rare. In addition, the finding of higher rates of hypocalcemia may be due to other factors (i.e. more treatments in the citrate group used thawed plasma).

Abstract Category: C) RRT Technique Characteristics

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Single Center US Experience Using a Dedicated Pediatric Sized Filter Set for Children

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PURPOSE: During the COVID19 pandemic, United States Food and Drug Administration [FDA] issued an emergency use authorization (EUA) for the use of Prismaflex HF20 set for children between 8-20 kg needing Continuous Kidney Support Therapy [CKST]. We report our experience of this hemofilter for CKST at a quaternary care freestanding pediatric hospital.

METHODS: Prospective CKST related data collection via our institutional automated dashboard between June 1st and November 30th 2021. Additional variables including patient demographics, underlying diagnoses, laboratory values and parameters for dialytic therapy were collected through manual chart review.

RESULTS: Of the 23 patients who had CKST during the study period, 9 (67% male) were treated for a total of 131 CKST days with HF20. Age range was between 1-9 years. The underlying diagnoses included complex congenital heart disease (3), liver failure (3), bone marrow transplant (2) and septic shock (1). All children received continuous venovenous hemodiafiltration with prefilter dilution and regional citrate anticoagulation. Only 3 patients required blood prime. Average filter life was 54.64 h (range 16-88 h). Median dialysis catheter size at start was 8 Fr [range 7-10 Fr]. The median initial blood flow rate was 40 ml/h [IQR 30-70]. Of the 75 filters, majority were changed as scheduled (64%), 13% clotted, 12% stopped for procedures, 8% access problem, 3% machine malfunction. The mean prescribed clearance was 102 ± 16 ml/kg/h and the delivered clearance was 68 ± 8 ml/kg/h. There were no major adverse events.

CONCLUSION: HF20 filter delivers efficacious CKST to younger children with AKI. The smaller priming volume and safety profile makes it a valuable addition to available therapies for kidney support in this vulnerable population. Monitoring delivered dose may be an important consideration to optimize metabolic control.

Abstract Category: C) RRT Technique Characteristics

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Acute Peritoneal Dialysis and Intermittent Hemodialysis in Patients with Acute Kidney Injury Requiring Renal Replacement Therapy: A Randomized Controlled Trial

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Background: Modalities in acute kidney injury (AKI) requiring renal replacement therapy (RRT), there is no consensus on whether conventional intermittent hemodialysis (IHD) or peritoneal dialysis (PD) is the preferable option. In resource-limited setting, acute PD is a preferred option of RRT due to its technically simple procedure. This study aimed to compare short- and long-term outcomes of AKI patients between IHD and acute PD.

Methods: A multicenter randomized controlled trial compared the outcome between IHD (three times a week) and acute PD (18-24 liters per day) from May 2018 to January 2021 in AKI patients. The primary outcome was a 28-day in-hospital survival rate. Secondary outcomes included 28-day renal recovery and dialysis dependence, duration of ICU period, 6-month in-hospital survival rate, renal recovery, and dialysis dependence.

Results: We included 100 patients (47 allocated to acute IHD and 53 to PD). Before RRT initiation, baseline clinical characteristics between groups were comparable. Overall mean age 54.6 ± 15.9 years old. The main cause of AKI was sepsis (70%). There was no difference in the 28-day hospital survival rate between IHD and acute PD (51.06 vs 49.06 %, p=0.84), 28-day dialysis dependence (14.89 vs 7.55 %, p=0.24). Hospital survival rate and dialysis dependence at 6 months were similar between IHD and acute PD patients (36.17 vs 28.30%, p=0.39, 8.51 vs 5.66%, p=0.58). A Cox proportional hazards model demonstrated a nonsignificant difference between the mode of dialysis and survival rate (hazard ratio, 1.29; p=0.44).

Conclusion: In AKI patients requiring renal replacement therapy, acute PD showed comparable outcome to IHD.

Abstract Category: C) RRT Technique Characteristics

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Piperacillin/Tazobactam Dosing Suggestions In Critically Ill Patients with Continuous Renal Replacement Therapy

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Background: Acute kidney injury in critically ill patients is primarily caused by sepsis and treated by continuous renal replacement therapy (CRRT). Piperacillin/Tazobactam (PIP/TAZ) is a beta-lactam antibiotic used to manage nosocomial infections especially from Pseudomonas aeruginosa. Owing to its pharmacokinetics, this drug is significantly removed via CRRT and needed to consider drug dosing adjustment.

Methods: A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P). We searched PubMed, Embase and ScienceDirect from inception to December 2020 with set inclusion and exclusion criteria. All study selection, data extraction and risk of bias assessments were independently performed by three researchers. Screening identified 219 articles of which 9 were included. Pharmacokinetic (PK) models were developed using published PK data with systematical approach in critically ill patient with known variability. Monte Carlo simulation was used to develop optimal dosing recommendations. Two CRRT modalities of continuous hemofiltration (CH) and continuous hemodialysis (CHD) and effluent flow rates of 25 and 35 mL/kg/h were utilized in the models. PIP/TAZ regimens were evaluated on the probability of target attainment (PTA) using %fT>MIC & %fT>4MIC > 50% for Pseudomonas aeruginosa (MIC breakpoint from CLSI of 16 mg/L) for the initial 48 hours-therapy. Optimal dosages were defined from regimens that yielded a PTA > 90% with smallest daily dose.

Results: With standard target of 50%fT>MIC, the optimal daily regimen of 2 g loading dose followed by 1 g every 8 hours was recommended for both modalities with the effluent rates of 25 and 35 mL/kg/h. When the aggressive target of 50%fT>4MIC was applied in the models, the regimen of 12 g/day was needed in patients receiving CH with both effluent rates. Patients receiving CHD with the effluent flow rate of 25 mL/kg/h needed 12 g/day while the larger dose was required as 16 g/day in patients receiving the effluent rate of 35 mL/kg/h. In addition, we also performed the PTAs of each dosing regimen with varying the MICs for drug dosing modification in different clincial settings which reported lower MICs compared with CLSI.

Conclusion: CRRT modalities, effluent flow rates and pharmacodynamic targets considerably contributed drug dosing adjustment. Clinical validation of these recommendation is required.

Abstract Category: D) RRT Applications and Targeted Interventions

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Evaluation of Linezolid Dosing Regimens in Critically Ill Patients Using Monte Carlo Simulation

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Background: The septic critically ill patients have pharmacokinetics (PK) changes in terms of higher volume of distribution (Vd) and higher clearance. Linezolid has a low molecular weight, moderate Vd and low protein binding. Hence, it would be sub-therapeutic in this population and could be removed by continuous renal replacement therapy (CRRT). In addition, the optimal linezolid dosing regimens in the critically ill patients based on PK and pharmacodynamic concepts are not well established. This study aimed to define the optimal dosing linezolid regimens in these patients by using the Monte Carlo simulation.

Methods: A one-compartment pharmacokinetic model was conducted to predict linezolid concentrations for the initial 72 hours of therapy. Effluent rates as ultrafiltration and dialysate flow rates of 25 and 35 mL/kg/h were used in the models. The pharmacodynamic target of AUC24h/MIC > 80 which the MICs varies from 0.5-4 mg/L were applied to evaluate efficacy. The dose that achieved > 90% of the probability of target attainment were defined as an optimal dose.

Results: The results of this study showed the standard dosing regimen (600 mg q 12 h) was not sufficient for MRSA infection with MIC > 2 mg/L and 1 mg/L in critically ill patients with and without receiving CRRT, respectively. The optimal dose of linezolid for MRSA infection with MIC 0.5 mg/L in critically ill patients with and without receiving CRRT is 300 mg q 12 h and 600 mg q 12 h, respectively. For achieving the higher MIC pathogens, the higher dose of linezolid was needed to achieve the target goal. (Table 1)

Conclusions: The pathogen MIC plays a major contribution to linezolid dosing. CRRT modalities with recommended effluent rates did not alter dose modifications. Alternative antimicrobial agents would be considered when treating MRSA infection with MIC > 1 mg/L in critically ill patients and MIC > 2 mg/L in patients undergoing CRRT. Clinical validation of these recommendations is required.

Table on following page

MIC (mg/L)	Critically ill patients	Critically ill patient undergoing CRRT (CVVH, effluent rate 25 mL/kg/h)
0.5	600 mg q 12 h	300 mg q 12 h
1	600 mg q 8 h	600 mg q 12 h
2	1,800 mg q 12 h*	600 mg q 8 h*
4	2,400 mg q 8 h*	1,200 mg q 8 h*
* Alternative antimicrobial agents would be considered.		

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Serum Potassium as A Mortality Predictor Among Patients Requiring Continuous Renal Replacement Therapy

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Background
Hyperkalemia and hypokalemia are common events in critically ill patients requiring continuous renal replacement therapy (CRRT). Mortality among patients with AKI significantly increases with any form of kidney replacement therapy. The particular impact of either hypokalemia or hyperkalemia on outcomes depends on several factors, including acute illness and underlying comorbid conditions. A U-shape association with mortality in non-dialysis patients has been reported, yet the values at which any medical or extracorporeal (KRT) intervention is warranted are not well established. Therefore, the optimal serum potassium level at which the benefits of CRRT outweigh its risks is still unknown. We aimed to assess the association between serum potassium before and during CRRT with mortality.

Methods:
This is a retrospective cohort involving 1,279 critically ill patients of a tertiary center in the US receiving CRRT (CVVH) for AKI from December 2006 through November 2015. Patients who had end-stage kidney disease were on dialysis before CRRT initiation or received CRRT for less than 24 hours were excluded. The standard dose prescribed was 30 ml/kg/hr, and the replacement fluid contained 4 mmol/L of potassium, although there was an option to adjust the potassium concentration from 2 to 6 mmol/L. We used logistic regression to assess serum potassium before CRRT and mean serum potassium during CRRT as predictors for 90-day mortality after CRRT initiation.

Results: Before CRRT, there was a U-shaped association between serum potassium and 90-day mortality, with the nadir of mortality noted in serum potassium of 4.0-4.4 mmol/L (Fig 1). In adjusted analysis, there was a significant increase in mortality when serum potassium before CRRT was ≤3.4 and ≥4.5 mmol/L, compared to serum potassium of 4.0-4.4 mmol/L. In contrast, during CRRT, mortality progressively increased when the mean serum potassium was ≥4.5 mmol/L Fig 2). In adjusted analysis, mean serum potassium ≥4.5 mmol/L had 1.61-time higher odds of 90-day mortality than mean serum potassium 4.0-4.4 mmol/L.

Conclusion: Hypokalemia and hyperkalemia before CRRT and hyperkalemia during CRRT predicts 90-day mortality. During CRRT, mean serum potassium ≥4.5 mmol/L was associated with increased mortality risk.

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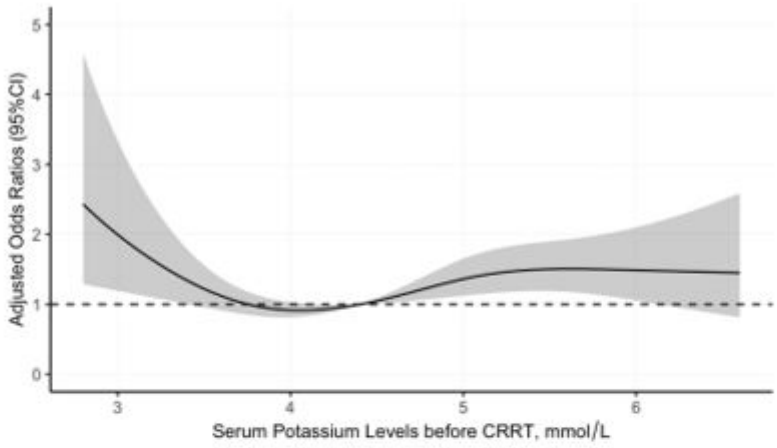

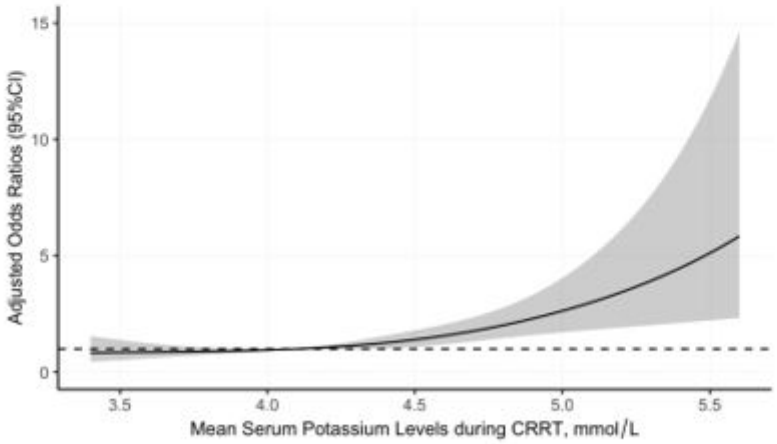

Abstract Category: D) RRT Applications and Targeted Interventions

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Economic Evaluation of the TherMax Blood Warmer for Reducing Hypothermia Episodes During CRRT

Jorge Echeverri[1], Max Bell[2], Michael J Blackowicz[1], Kai Harenski[1], Marcus Broman[3]

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Hypothermia is common in patients with AKI who are treated with continuous renal replacement therapy (CRRT) and can have adverse clinical consequences. The TherMax blood warmer (Baxter Healthcare), which is integrated with the PrisMax device (Baxter Healthcare) to deliver CRRT, maintains prescribed temperature targets by directly warming the blood with heating plates and adjusting warming based on estimated return blood temperature and CRRT prescription parameters. It has been shown to reduce the occurrence of hypothermia. The objectives of this study were to estimate and compare the risk of hypothermia and the costs and cost-effectiveness associated with the TherMax blood warmer versus a standalone CRRT blood warmer.

An economic model was developed in which relevant health states for each treatment were normothermia, hypothermia, discharge, and death. Clinical inputs were obtained before and after an ICU switched from the Barkey S-Line standalone blood warmer (Barkey GMBH & Co KG) used in conjunction with the Prismaflex system (Baxter Healthcare) to the TherMax blood warmer integrated with the PrisMax system. Data were obtained from 526 patients who were treated with the Prismaflex system and the standalone blood warmer (median 62 hours [8.9 days] per admission) prior to November 2018. After November 2018, 29 patients were treated with the PrisMax system and the TherMax blood warmer (median of 68 hours [9.7 days] per admission). Primary model inputs for both warmers were age (65.4 years), life-years remaining – US population age 65 (17.5), life-years remaining – ESRD on dialysis age 65 (7.8), and chronic dialysis (21.8%). Hypothermia occurred in 34.5% of patient with the TherMax warmer and 71.9% of patients with the standalone warmer. Mortality was 40% among normothermic patients and 59.2% among hypothermic patients. Costs were obtained from publically available summary estimates.

Cost per life-year gained ($8,615 in the TherMax warmer group and $10,115 in the standalone warmer group) resulted in a negative incremental cost-effectiveness ratio, indicating greater cost-effectiveness for the TherMax device compared to the standalone warmer (Figure 1). The TherMax blood warming device used with the PrisMax system was associated with a lower risk of hypothermia, which our model indicates leads to lower costs, more life-years gained due to avoidance of death due to hypothermia, and greater cost-effectiveness.

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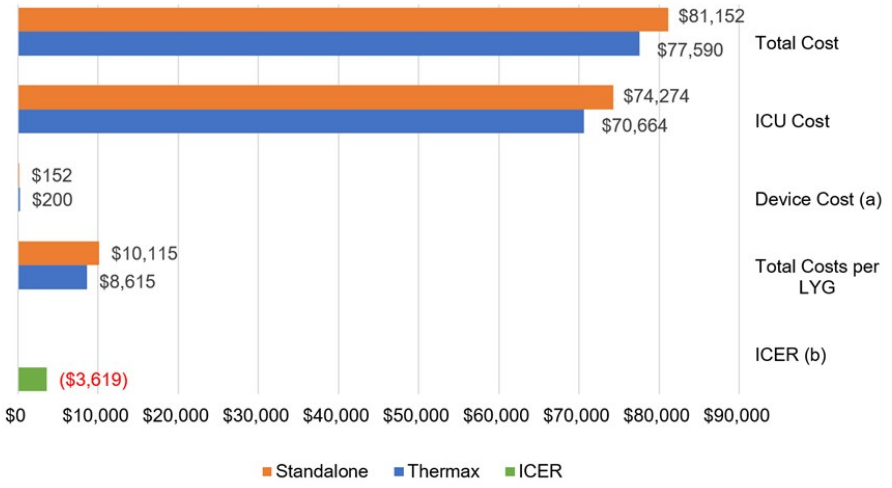
Figure 1. Cost-effectiveness results



Costs are in 2020 US Dollars.
Cost of CRRT was $6,727 in both warmer scenarios.
Life-years gained (LYG): 9 with the Thermax warmer vs 8 with the standalone warmer.
(a) Device cost per patient = (device list price) / (365 days per year) / (7 days per patient) x (80% use efficiency).
(b) Incremental cost-effectiveness ratio (ICER) = difference in total cost / difference in LYG; the green bar represents a negative number for the ICER result, indicating a greater cost-effectivenes of the Thermax blood warmer.

Abstract Category: D) RRT Applications and Targeted Interventions

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First-time Use of the Seraph® 100 Microbind® Affinity Blood Filter in a Pediatric Patient with Severe COVID-19 Disease: A Case Report

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Background: The Seraph® 100 Microbind® Affinity Blood Filter is a broad-spectrum sorbent hemoperfusion device designed to reduce bacteria, viruses, toxins, cytokines, and other inflammatory mediators. As an extracorporeal therapy, it can be added in-line to both continuous kidney replacement therapy (CKRT) and extracorporeal membrane oxygenation (ECMO). The FDA granted an emergency use authorization (EUA) for the Seraph® 100 in adults admitted to the ICU with respiratory failure. Early studies show the device is safe in adults and may reduce morbidity and mortality. This filter has not previously been used in children.

Case: A 17-year-old 180kg child with asthma presented to the emergency department (ED) with respiratory distress due to COVID-19 infection requiring bi-level positive airway pressure (BiPAP) and Pediatric Intensive Care Unit (ICU) admission. His course was complicated by severe rhabdomyolysis, KDIGO stage 3 acute kidney injury (AKI) (serum creatinine >10 mg/dL and oliguria). He received dexamethasone, remdesivir and one dose of tocilizumab. He was initiated on CKRT on ICU day 2. On day 3, His respiratory status declined, requiring intubation and escalation of ventilator settings for possible pulmonary hypertension crisis. His clinical picture continued to worsen on ICU day 4, leading to discussion of ECMO and prone positioning.

Under FDA emergency device use approval, The Seraph® 100 filter was added to his extracorporeal circuit on ICU day 4. He had transient hypotension starting ~5 minutes after initiation of CKRT with the Seraph filter requiring increase in vasoactive support that lasted about 5 minutes until returning to baseline level. He was continued on CKRT and treated with a total of 3 individual filters from ICU day 4 to 8. During this time, his respiratory status improved, vasoactive medication requirement decreased, and inflammatory markers decreased (Table 1). He was extubated on ICU day 8 and CKRT was discontinued. He did not require further kidney replacement therapy. He was discharged on hospital day 23 with a creatinine of 1.65mg/dL.

Conclusion: This pediatric patient with severe COVID-19 ARDS and stage 3 AKI requiring CKRT tolerated treatment with the Seraph® 100 Microbind® Affinity Blood filter without any significant adverse events.

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Table 1. Trend of Cardiorespiratory Support Needed and Laboratory Markers

	ICU Day 3	ICU Day 4	ICU Day 5	ICU Day 6	ICU Day 7	ICU Day 8	ICU Day 9
Seraph Filter	**|---Filter #1 ---| |---------Filter #2----------| |----Filter #3-----|**						
Lowest PaO_2:FiO_2 Ratio	101.0	124.6	136.7	141.7	191.4	171.4	
Highest Oxygenation Index	19.3	14.4	13.2	12.7	6.2	6.4	
Mean Oxygenation Index	16.2	12.1	10.7	8.7	5.3	5.8	
Highest Norepinephrine Dose (mcg/min)	7.5	4	8	2	1	0	0
Cumulative Daily Dose (mcg)	1,432	5,124	3,119	2,435	657	0	0
Mean Norepinephrine Dose (mcg/min)	2.4	3.6	2.2	1.7	0.7	0	0
pSOFA Score	10	10	9	8	8	6	4
Troponin		257.74	164.57	89.52	49.86		19.74
CRP		7.90	4.60	3.00	1.90		0.60
Procalcitonin		5.05	3.46	1.54	0.87		0.38
Ferritin		775.0	643.7	890.5	936.7		505.6
CPK		1,300	1,099	721	782		490

Abstract Category: D) RRT Applications and Targeted Interventions

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No Water, No Problem: Using CRRT For Hemodialysis Patients

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Introduction:
Each dialysis session uses approximately 150 to 200 L of water. While this was an issue discussed by policymakers and environmentalists, the winter storm that swept across the southwest United States in February 2021 made the bedside physician keenly aware of the problem.

The region saw an unprecedented disruption of water and power supplies which put end-stage renal disease (ESRD) patients in jeopardy. Intermittent hemodialysis (IHD) could not be performed due to lack of running water, low water pressures, and unsanitary water conditions. We present 4 cases when continuous renal replacement therapy (CRRT) was utilized to provide urgent hemodialysis in hemodynamically stable, non-critically ill ESRD patients during this time of water supply crisis.

Case Presentation:
Our patients were between the ages 47-62 years old. All patients were ESRD patients on IHD 3 days per week. Shortness of breath was the presenting complaint in 3 of 4 patients, each of whom had missed their last scheduled HD session due to inclement weather. 1 of 4 patients presented with altered mental status. Indications for hemodialysis included volume overload with pulmonary edema, hypertensive crisis, refractory hyperkalemia, and uremic encephalopathy.

The CRRT equipment used included the PRISMAX system for CRRT with M150 filters. Renal replacement solution containing 32 mEq/L bicarbonate, 4 mEq/L potassium, and 2.5 mEq/L calcium was used as dialysate fluid. Continuous veno-venous hemodialysis (CVVHD) more was used with a dialysate flow rate of 6L/hour and a blood flow rate of 200/per hour with calculated urea clearance of 100 ml/min. The duration of treatment was 8 hours to achieve the target Kt/V of 1.15, comparable to the recommended 1.2 provided by IHD. 9-10 bags of dialysate were used per each session. Fluid removal ranged from 150-500 ml/hr. All patients tolerated the procedure well with the resolution of their acute conditions and normalization of blood pressure and electrolytes. 1 patient developed brief hypotension which resolved with fluid administration. No other adverse events were seen.

Discussion:
CRRT has typically been used for renal replacement therapy in critically ill patients. We demonstrate limited CRRT as an alternative to safely manage ESRD patients needing urgent hemodialysis in the scenario of a natural disaster resulting in a water outage.

Table on following page

Table 1: Patient characteristics, dialysis indication and CRRT prescription

	Patient 1	Patient 2	Patient 3	Patient 4
Age (in years), Sex	47, Male	49, Female	66, Male	62, Male
Co-morbidities	Insulin dependent diabetes mellitus, Hypertension, Heart failure Hyperlipidemia, anemia	Heart failure, Atrial fibrillation	Hypertension, Pulmonary Hypertension	Atrial septal defect, Multiple Myeloma
Indication	Fluid overload with pulmonary edema	Hyperkalemia	Uremic encephalopathy	Fluid overload, hypertensive crisis, pulmonary edema
Access	Tunneled dialysis catheter	Tunneled hemodialysis catheter	AV fistula	AV graft
Mode, blood flow rate, dialysate flow rate (in cc/hr),	CVVHD, 200, 6000	Day 1: CVVHD, 200, 6000 Day 2: CVVHDF, 150, 5000	CVVHD, 200, 6000	CVVHD, 200, 6000
Net fluid removal (in cc/hr)	200	Day 1: 200 Day 2:130-200	400	500
Duration (in hours)	8	Day 1: 4 Day 2: 8	8	8

Abstract Category: D) RRT Applications and Targeted Interventions

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The use of the novel Tablo Hemodialysis System to treat life-threatening hyperkalemia: a retrospective case series

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[1]*University of New Mexico School of Medicine,* [2]*Outset Medical*

Introduction
The Tablo Hemodialysis (HD) System (Outset Medical) is a next-generation, self-contained HD device approved by the FDA in 2016. Tablo has an integrated reverse osmosis system with the ability to produce dialysate on demand, allowing for use in any location with a potable water source. This, and the small device footprint, results in increased portability, leading to our institutional adoption of Tablo as our default portable intermittent HD (IHD) device. The maximum dialysate rate (Qd) allowed by Tablo is 300 mL/min. This study was conducted to assess Tablo's ability, at a Qd of 300 mL/min, to provide the rapid solute clearance needed to treat severe hyperkalemia.

Methods
We carried out a retrospective review of all treatments using Tablo at the University of New Mexico Hospital (UNMH) from May 1, 2020, to September 30, 2021. A total of 473 admissions with at least 1 Tablo treatment were screened. 77 patients with a peak serum K of >/= 6.5 mEq/L were identified. We excluded 26 treated with medical therapy resulting in K <6.5 mEq/L prior to HD, 20 treated with another device [continuous renal replacement therapy (CRRT) or traditional IHD] before Tablo, 5 treated with Tablo for <3h, and 4 with incomplete records, yielding 22 patients for final analysis.

Results
The patient and prescription details for the treatments are in Table 1. All 22 HD sessions used a Revaclear 300 dialyzer (Baxter) and 20/22 used a 2 mEq/L K bath. With a mean treatment length of 3h 55 min +/- (standard deviation) 25 min and mean Qb of 361 +/- 41 mL/min, a mean pre-HD K of 7.0 +/- 0.4 mEq/L was lowered to a mean post-HD K within the normal range at 4.7 +/- 0.7 mEq/L.

Limitations
Intervals between K measurement and HD initiation and discontinuation were variable as all data were from usual care. Also, non-dialytic changes in K balance were not captured.

Conclusion
These data suggest that HD with Tablo using a standard high-flux dialyzer and a Qd of 300 mL/min can be effective in the emergent treatment of life-threatening hyperkalemia. While at UNMH we use portable Tablo treatments to complement our ICU-based CRRT program and the traditional IHD machines in our acute HD unit, Tablo can be used to provide the full RRT spectrum from continuous 24-hour therapy to standard IHD. This study is especially relevant to centers with a Tablo-only program as it shows that Tablo can readily achieve the standard of care for patients requiring emergent dialytic treatment of hyperkalemia.

Table on following page

Subject Number	Age (years)	Gender	AKI or ESKD	Pre-HD weight (kg)	Pre-HD K (mEq/L)	Interval from pre-HD K to HD (h:mm)	Treatment Duration (h:mm)	Post-HD K (mEq/L)	Interval from HD to post-HD K (h:mm)	Change in K (mEq/L)	UF (mL)	HD Access	Qb (mL/min)	Qd (mL/min)	K bath (mEq/L)
1	52	M	ESKD	100.3	6.6	0:10	3:32	4.6	2:02	-2.0	4000	fistula	400	300	2
2	48	M	ESKD	102.5	7.7	3:55	3:49	5.5	8:41	-2.2	4000	fistula	400	300§	2
3	54	M	ESKD	87.9	6.9	3:54	4:03	4.2	0:37	-2.7	2000	fistula	400	300	2
4	59	M	ESKD	76.3	6.6	2:17	4:16†	5.2*	5:38	-1.4	3900	fistula	361.7‡	300	2
5	63	M	ESKD	115.3	7.3	2:47	5:01	4.6	3:18	-2.7	480	fistula	355.5‡	300	2
6	65	M	ESKD	71.2	7.3	0:53	3:52	5.0	4:50	-2.3	0	fistula	350	300	2
7	64	F	ESKD	49.5	6.9	3:36	4:09	4.4	4:13	-2.5	1000	tunneled cath	338.0‡	300	2.15‡
8	46	M	ESKD	70.6	7.3*	6:23	3:58	5.1	0:17	-2.2	3000	tunneled cath	350	300	2
9	60	M	ESKD	111	6.6	2:48	4:05	5.9*	3:47	-0.7	1000	fistula	400	300	2
10	52	M	ESKD	114.7	6.5	6:08	4:00	3.8	0:40	-2.7	500	fistula	400	300	3.4‡
11	55	M	ESKD	74.4	7.3	1:08	4:17	4.4	8:37	-2.9	1500	fistula	400	300	2
12	49	M	ESKD	70.5	7.3	2:41	3:58	6.6	1:22	-0.7	0	fistula	300	300	2
13	67	M	ESKD	61.8	7.3	1:39	3:59	4.8	2:16	-2.5	1040	fistula	400	300	2
14	59	M	ESKD	122.3	6.6	2:25	4:14	4.6	9:26	-2.0	2100	fistula	400	300	2
15	78	F	AKI	81.1	6.9	0:27	3:26†	4.9	7:07	-2.0	-400	temporary cath	250	300	2
16	55	M	AKI	68.9	7.9	0:34	3:49	4.1	1:30	-3.8	-200	temporary cath	343.4‡	300	2
17	41	M	AKI	66.7	6.7	3:09	3:00	3.8	2:21	-2.9	1000	temporary cath	350	300	2
18	64	M	ESKD	74.1	6.6	1:38	3:40	4.1	2:08	-2.5	1810	temporary cath	350	300§	2
19	36	M	ESKD	61	6.5*	4:31	4:07	4.6	4:22	-1.9	1000	temporary cath	313.0‡	300	2
20	47	M	ESKD	76.6	6.8	6:12	4:00	3.9	4:36	-2.9	3990	tunneled cath	350	300§	2
21	64	F	AKI	133.4	6.7*	3:41	3:12	4.7	3:52	-2.0	0	temporary cath	331.0‡	300	2
22	79	M	AKI	50.9	7.5	6:34	3:42	5.4	12:28	-2.1	-100	temporary cath	400	200	2
Mean	57.1			83.7	7.0	3:04	3:55	4.7	4:17	-2.3	1437		361.0	295.5	2.07
Std Dev	±10.7			±23.8	±0.4	±1:59	±0:25	±0.7	±3:14	±0.7	±1486		±40.5	±22.4	±0.3

*blood samples with slight-to-moderate hemolysis.

†treatments 4 and 15 were interrupted by 29- and 24-minute stoppages; reported time excludes interval off treatment.

‡treatment parameter was adjusted during treatment; time-weighted average reported.

§treatments 2, 18, and 20 had charted Qb >300 mL/min, which is impossible with Tablo; these Qb rates are presumed to be erroneously recorded and max Qb of 300 is reported.

AKI, acute kidney injury; cath, catheter; ESKD, end-stage kidney disease; HD, hemodialysis; Qb, blood flow rate; Qd, dialysate rate; Std Dev, standard deviation; UF, ultrafiltration (positive is volume removed).

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Severe Lithium Toxicity Treated with the Tablo Hemodialysis System: A Case Report

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Introduction:
Lithium has a very narrow therapeutic window, and toxicity is common for those on chronic lithium treatment. Hemodialysis has been recommended by EXTRIP for symptomatic cases of lithium toxicity with levels >4meq/L with renal failure. Rebound of serum lithium levels is common after intermittent HD and may require additional dialysis to achieve clinical goals. We describe a case of severe symptomatic lithium toxicity treated with the Tablo hemodialysis system ("Tablo"), the first reported case using the novel device.

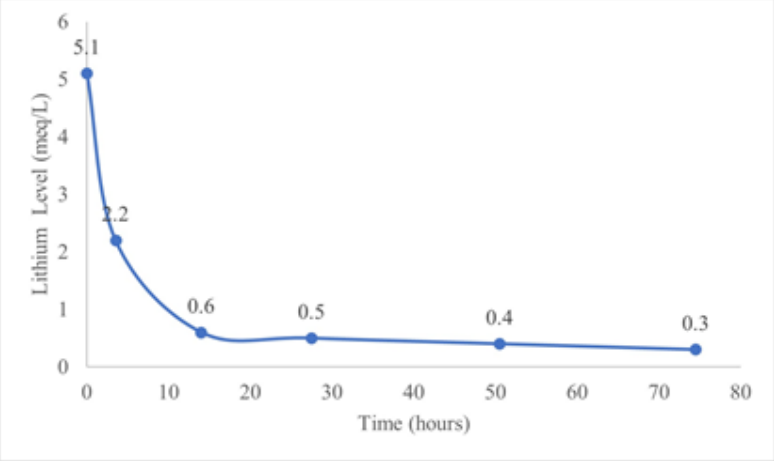
Tablo is approved for use in hospitals, in-center, and patient homes. It has a number of advantages, including the ability to utilize tap water for dialysate, ease of use, and increased portability. It was recently adopted at Bronson Methodist Hospital as the default dialysis machine for all treatments in the ICU.

Methods:
A 54-year-old female with a past medical history of bipolar disorder treated with lithium presented with worsening mental status. She reported confusion 5 days prior to admission and developed intractable muscle contraction, visual hallucinations, and decreased urine output despite decreasing her lithium dosing.
A serum lithium level of 5.1meq/L confirmed the diagnosis of lithium toxicity. Patient was also in acute renal failure with a creatinine level of 2.27 mg/dL. The patient was prescribed dialysis in the ICU with Tablo for a total runtime of 22 hours . The treatment was performed through a temporary catheter and utilized a blood flow rate of 400 mL/min, and dialysate flow rate of 90 mL/min, and Optiflux F160NR dialyzer. Lithium levels were drawn at presentation, 6 hrs, 12 hrs, and post-treatment.

Results:
The patient experienced rapid improvement in clinical symptoms with dialysis. Lithium levels (Figure 1), declined from 5.1meq/L to 2.2meq/L within 6 hours of therapy. A lithium level of 0.6meq/L was obtained at 12 hours. Lithium 6 hours after treatment demonstrated a stable lithium level of 0.5 meq/L, with no evidence of rebound through 48 hours. The patient was asymptomatic post dialysis and was discharged on day 5.

Conclusion:
This is the first reported use of Tablo for treatment of lithium toxicity. Tablo can effectively treat lithium toxicity with rapid achievement of clinical and therapeutic goals with a single treatment without evidence of rebound.

Figure on following page



Abstract Category: D) RRT Applications and Targeted Interventions

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Continuous Renal Replacement Therapy as a Novel Therapy for Management of Aluminum Phosphide Poisoning

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Purpose of the study: Aluminium phosphide (AP) poisoning is very common in India and carries a high mortality with no established modality of treatment or antidote. We present a retrospective analysis of Aluminum phosphide poisoning in last 1 year at a tertiary care hospital in North India and demonstrate the usefulness of early initiation of CRRT in such cases.

Methods used: We retrospectively analyzed 140 poisoning cases out of which 36 AP poisoning cases were identified and cases that received CRRT were compared with those managed conservatively for survival, inotropic requirement, AKI, lactic acidosis, ECHO findings, time of presentation to ER and to CRRT initiation. Since most of the patients could not define the quantity consumed, this criteria was excluded from the analysis. CRRT (CVVHDF) was done with a Fresenius multiFilterate machine using Primasol® (Baxter). The average delivered dose was 30 ml/Kg/hr. Replacement flow rates were kept at an average of 1600 ml/hour and dialysate 1000 ml/hour. CRRT was discontinued once serum lactate normalized, inotrope requirements improved and hemodynamic stability was achieved.

Summary of the result: Incidence of AP poisoning was 25.7%. Patients having lactates of more than 1.0mmol/L, depressed ejection fraction(EF), requirements of inotropes and AKI were offered CRRT and 9 out of 35 patients opted for it. In the CRRT arm, 4 out of 9 survived (44.4%) vs 7 out of 26 (26.9%) in conservative arm. In the conservative arm, average time to ER after AP poisoning was 45 minutes in all survivors vs 4.5 hours in 12 out of 17 deceased. Amongst survivors 4 out of 7 were hemodynamically stable with normal lactates, no inotropes, normal EF and 1 out of 7 (14%) had AKI . All the deceased (19) had progressively worsening lactates, required inotropes, had low EF and 17 out of 19 deceased (89.4%) had AKI. In the CRRT arm, all 9 cases had inotrope requirements, depressed EF and progressively rising lactate. All 4 survivors presented to ER in an average 50 minutes and CRRT initiated in 5.5 hours compared to the deceased where average time to ER was 2.5 hours and CRRT initiated in 11 hours. AKI was observed in 4 out of 5 deceased (80%) and 1 out of 4 survivors(25%).

Conclusion: With CRRT, mortality benefits could be achieved. Factors favoring the outcome were early presentation to ER and early CRRT initiation. Absence of AKI, lactic acidosis and myocardial depression requiring inotropic support gave better chances of survival.

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Single Pass Albumin Dialysis (SPAD): Effects of Dialysate Albumin Concentration, Dialysate Flow Rate and Hemofilter Membrane

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Introduction: Acute liver failure is associated with high mortality without liver transplant. Extracorporeal liver support, either as a bridge to transplant or recovery, is frequently indicated. Unlike water-soluble uremic toxins albumin-bound liver toxins are not well depurated by continuous kidney replacement therapy (CKRT). Modifying CKRT dialysate by adding human albumin has been shown to enhance removal of bilirubin and bile acids. Bound-solute dialysis, with single pass albumin dialysis (SPAD), retains interest as a supportive therapy due to its simpler cost effective set up and easy availability. However, reports on SPAD have not reached a consensus on the suggested optimal albumin concentration, dialysate flow rate, hemofilter membrane, as well as other factors to consider when removing albumin-bound toxins.

Purpose of the study: The purpose of this audit was to evaluate the effect of dialysate albumin concentration and dialysate flow rate on the removal of bilirubin, a surrogate marker for albumin-bound liver toxins.

Methods: Review of record of patients who were planned for or who underwent SPAD for acute or acute on chronic liver failure over the past 3 months.

Results: Four patients (of which 3 patients underwent SPAD) were included in the review (Figure 1). The first patient (1*) was planned for, but did not undergo SPAD. The other three patients underwent a session of SPAD but all of them ultimately decided for maximal medical management and withdrawal of aggressive supportive treatments. The rate of bilirubin removal was greater with SPAD. Dialysate with albumin concentration of 3.3% had the highest removal rate per liter of effluent.

Conclusion: SPAD had greater bilirubin removal as compared to conventional CKRT. 3.3% albumin concentration in the dialysate offered greater bilirubin removal than dialysate albumin concentration of 1.8%. The influence of the dialysate flow rate, CKRT modality and hemofilter membrane on bilirubin removal are unclear. Larger studies to determine ideal albumin concentration, dialysate flow rate and hemofilter membrane are needed to optimize the use of SPAD in removing albumin-bound toxins.

Table on following page

Patient	1*	2	3	4
Dialyzer (Surface Area in Square Meter)	oXiris (1.5)	AV1000S (1.8)	M100 (0.9)	M100 (0.9)
Membrane	Modified AN69	Polysulfone	AN69	AN69
CKRT Modality	CVVHDF	CVVHD	CVVHDF	CVVHD
Effluent Flow Rate (Dialysate flow rate in CVVHDF)	3L/hour (1.8L/hour)	2.5L/hour	3L/hour (1L/hour)	2L/hour
Dialysate Albumin Concentration	None	1.8%	1.8%	3.3%
Duration	Not applicable	4 hours	6 hours	8 hours
Bilirubin Removal per Liter of Effluent	0.29mg/L	5.4 mg/L	10.5mg/L	16.4 mg/L
Bilirubin Removal Rate per Minute	0.0145mg/min	0.220 mg/min	0.525mg/min	0.545mg/min

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Treatment with CRRT and adsorbent column (CytoSorb) in a patient with hyperinflammatory syndrome and multiple organ dysfunction due to hemophagocytic lymphohistiocytosis.

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Previously healthy 51-year-old Mexican patient who presented flu-like symptoms with fever, headache, arthralgia, jaundice, and hemato-splenomegaly.

• Presentation of the case
He was admitted to the intensive care unit, with APACHE II of 20 points, mortality 35.5%. Dengue hyperinflammatory shock was suspected, however serology and polymerase chain reaction were negative, as well as SARS-CoV-2 infection was ruled out. Due to oliguria and KDIGO 3 criteria for acute kidney injury it was decided to start Continuous Slow Renal Replacement Therapy (CRRT). During her evolution, she presented pancytopenia and coagulopathy, documenting hemophagocytic lymphohistiocytosis by bone marrow aspiration / biopsy. Due to the presence of hyperinflammatory shock, it was decided to add an adsorption column (cytosorb).

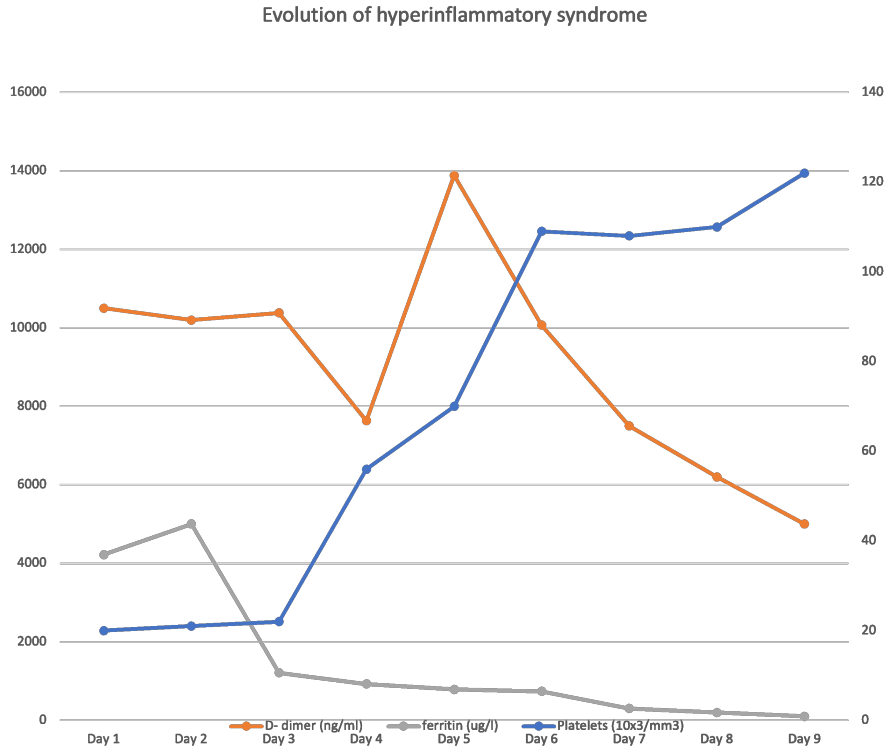
• Treatment
The patient received adsorption column renal replacement therapy on the second day of admission to the ICU. CRRT in CVVHDF modality, regional anticoagulation with citrate and with cytosorb hemoadsorption was used during the first two days. Continuing just CRRT for 4 more days. When having a bone marrow aspiration / biopsy result where hemophagocytic lymphohistiocytosis is documented (meeting biochemical criteria for elevated ferritin, coagulopathy, hypertriglyceridemia), dexamethasone and cyclosporine are added to the treatment.

• Evolution and results
Decreased inflammatory parameters and vasopressor requirement were observed during treatment with CRRT and hemaadsorption with cytosorb. Due to acute heart failure data attributed to myocarditis (increase in troponin T, NT-ProBNP, echocardiographic data), levosimendan was added and CRRT was continued with moderate ultrafiltration, with an adequate response.

Resolution of the hyperinflammatory syndrome and multiple organ dysfunction was achieved with successful extubation and complete recovery of renal function. I will be released from the intensive care unit after a 10-day stay.

Conclusion;
Hemophagocytic lymphohistiocytosis is characterized by an uncontrolled cytokine storm which causes multiple organ dysfunction with a generally fulminant course and high mortality. The viral panel was negative for dengue virus, SARS-CoV-2, HCV, HBV, HIV, cytomegalovirus,

parvovirus B19, Epstein Barr virus. We present a case of hyperinflammatory shock and hemophagocytic lymphohistocytosis that was successfully treated with renal support therapy and hemoadsorption column as part of multidisciplinary management.



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Implementation of an Automated AKI Risk Stratification Algorithm is Associated with Improved Outcomes in Critically Ill Children Receiving CKRT

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Starting 7/2017, an acute kidney injury (AKI) risk stratification algorithm, TAKING FOCUS 2 (TF2) was implemented in our PICU. TF2 uses Renal Angina Index (RAI) directed NGAL measurement for clinical decision support to mitigate 20% fluid overload from ICU admission (%FO). The RAI automatically results 12 hours after ICU admission, and an order for NGAL is reflexively placed for RAI≥8 in our electronic health record. Here we analyze continuous kidney replacement therapy (CKRT) trends and outcomes between the eras before (preTF2) and after TF2 implementation to assess for associations between the TF2 algorithm and outcomes.

We started collecting data from pts receiving CKRT in 2013 as part of our QI program. %FO data were added in 03/15. Variables include PRISM III scores, days from ICU admission to CKRT start, %FO at CKRT start, days on CKRT, survival to CKRT liberation, survival to ICU discharge, and ICU length of stay (LOS). Mann Whitney U tests were used for all non-normally distributed continuous data; Pearson chi-squared tests were used for all categorical data, with p-value <0.05 considered significant. A multivariable (MV) logistic regression model was developed to include variables associated with outcomes on bivariate analysis with $p<0.20$, to assess for incremental associations between the variables and outcomes.

Data from 268 PICU pts admitted between 01/2013 and 09/2021 were analyzed (pre-TF2:106, TF2:162). Neither pt. age nor weight differed between era cohorts. The pre-TF2 era cohort had higher PRISM III scores, started CKRT later, and had higher %FO at CKRT start. Pts in the TF2 era received CKRT for shorter duration, had shorter duration between CKRT liberation and ICU discharge, and a shorter overall ICU LOS. The PICU survival rate was higher in the TF2 era. A MV logistic regression model (era, PRISM III, days from ICU admission to CKRT start, %FO) revealed only TF2 era retained association with ICU mortality (aOR:4.4, 95%CI 2.1-9.1, $p<0.001$).

We observed 4+ year persistent association between TF2 implementation and improvement in CKRT outcomes in our PICU, including survival to ICU discharge. Given the association between TF2 and shorter CKRT duration/ICU LOS, we suggest the TF2 algorithm has potential to reduce healthcare costs.

Table on following page

Era	PRISM III[a]	ICU admit to CKRT Start [a] (days)	%FO at CKRT Start[a]	CKRT Duration[a] (days)	Survival to CKRT DC (%)	ICU LOS[a]	Survival to ICU DC (%)
Pre-TF2	12.5 [9,18]	4 [2,11]	9.5 [4.5,10.6]	6.0 [2.7,13.2]	68/106 (64%)	21.5 [10,42]	51/106 (48%)
TF2	10 [6,15]	2 [3,8]	3.7 [0.4,12.4]	3.7 [1.4,9.4]	116/162 (72%)	13 [10,26]	110/162 (68%)
p-value	0.014	0.0002	0.0001	0.005	0.19	0.0001	0.001

a. Median [IQR]

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CRITICALLY ILL PATIENTS WITH COVID-19 PNEUMONIA REQUIRING RENAL REPLACEMENT THERAPY WITH OXIRIS MEMBRANE IN A THIRD LEVEL HOSPITAL IN NORTH-EAST MEXICO

Lilia Maria Rizo Topete[1], Paola Borbolla[1], Bruno Samaniego[1], Francisco Torres[1]

[1]*Hospital Christus Muguerza Alta Especialidad, UDEM.*

Background:5 to 10% of patients with AKI require RRT during their stay in the ICU. The mortality ranges from 30 to 70%. A common factor of these patients is hemodynamic instability. CRRT has provided a versatile tool for the care of critically ill patients with hemodynamic instability who needs RRT such as acid-base disorders, fluid and electrolyte abnormalities, uremia, or fluid overload. The CRRT presents different modalities and allows the use of different membranes and cartridges, used in patients with MOF and sepsis with different indication, based upon de basal disease and the need for extracorporeal support. Recently it has generated new strategies as a measure for the decrease of inflammatory cytosines and the CRRT has earned a place in the ICU during the SARS-CoV-2 pandemic. Currently, a mortality of 50% is described in the patient with critical Covid-19 and a decrease in it has been reported when they undergo CRRT with the use of the oXiris® membrane. Therefore, the following study was carried out to describe our experience with the oXiris® membrane in patients with Covid-19.

Methods: Observational, retrospective, and analytical study. 13 hospitalized in the ICU with Covid-19 with positive PCR test, who required CRRT with the oXiris® filter between January 2020 and August 2021. Sociodemographic data, number of days total hospital stay (EIH) and ICU; duration and specifications of the TRRC, and its outcome.

Results: 10 men (76.9%). The mean age was 59.4 ± 12.9 years. The most frequent comorbidities were hypertension (53.8%) and DM2(38.4%); in 7 and 5 patients, respectively. The mean EIH was 60.3 ± 44.9 and 45.8 ± 30 days in the ICU. The median duration of the days with CRRT was 8 (3-11). The main indication for the initiation of CRRT was anuria (61.5%), followed by fluid overload (23%) and uremia (15.4%). Of the total population, 4 (30.7%) recovered kidney function, 5 (38.4%) were discharged with intermittent hemodialysis, and 8 (61.5%) died. In the first 48 hours of the initiation of CRRT with oXiris® the vasopressor requirements decreases besides the creatinine and urea.

Conclusions: Despite the use of the oXiris® filter in the patient with critical covid-19, mortality exceeds 50%, even if there is a good response in hemodynamical improvement at the begging of the therapy. We consider that this outcome is dependent on multiple comorbidities and clinical situations not included, so its application should continue to be investigated.

Table on following page

	n(%)	Media ± Ed	Median (p25-p75)
MALE	10 (76.9)		
BMI		59.4 ± 12.9	
DM		32.5 ± 6.8	
HTA	7 (53.8)		
CKD	3 (23)		
Q-SOFA			2 (1.25 - 2)
DAYS IN TRRC			8 (3 - 11)

Abstract Category: D) RRT Applications and Targeted Interventions

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ECMO Experience with the Tablo Hemodialysis System

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[1]*St Marks Hospital*

Background:
The Tablo® Hemodialysis System (Tablo) is an all in one, easy-to-learn device featuring integrated water purification, on demand dialysate production, two-way wireless data transmission and approved for use in the acute, chronic, and home settings.
Extracorporeal membrane oxygenation (ECMO) is used in critically ill patients presenting with acute cardiac and/or pulmonary dysfunctions, who are at high risk of developing acute kidney injury and fluid overload. The combination of ECMO and renal replacement therapy (RRT) is vital to the survival of these patients.

The objective is to report on the experience delivering Tablo RRT through the ECMO circuit to critically ill patients requiring both therapies.

Methods:
We conducted a retrospective review of all ICU Tablo treatments. Cases where the patient received dialysis and ECMO were identified. Tablo data were collected via real-time transmission to a cloud-based, HIPAA compliant platform and reviewed by site staff. Treatments were analyzed for achievement of the prescribed treatment time, whether the user ended the treatment or the device directed the termination.

Results:
Seventeen (17) Tablo treatment days in three patients on ECMO were observed. All treatments were prescribed for 24hrs and performed with Tablo connected within the ECMO circuit via pigtail cannulas with stopcocks. Median achieved treatment time was 23.4 hours, with the average treatment achieving 89% of prescribed time.

A total of four treatments ended early and were split evenly between user (2) and device (2) directed terminations. All terminations were due to unresolvable venous and arterial pressure alarms associated with stopcock positioning during setup of Tablo within the ECMO circuit. Clinically significant alarms occurred at a rate of 1.8 alarms (±1.8) per treatment hour with a mean resolution time of 11 seconds (±7). Alarms were related to venous pressure (57%), arterial pressure (42%), and other (1%).

Conclusions:
Tablo can be successfully integrated within the ECMO circuit to complete treatments and optimize care provision for the sickest patients in the ICU while simplifying care for patients and nursing staff.

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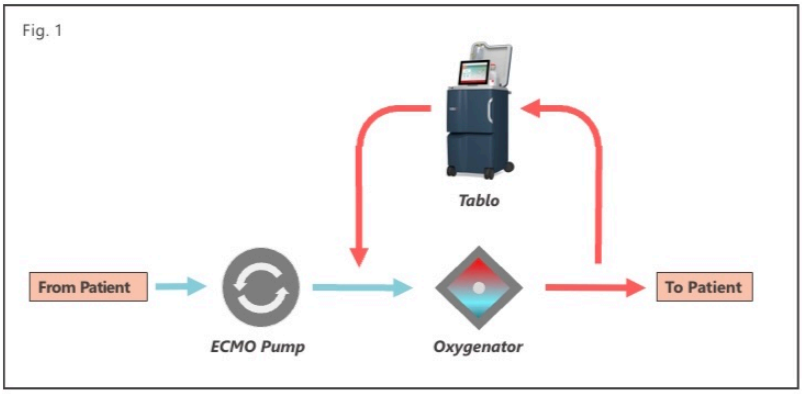

Abstract Category: D) RRT Applications and Targeted Interventions

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Continuous Kidney Support Therapy with Neonates Using the Carpediem System

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Purpose: Continuous kidney support therapy (CKST) delivery to small infants is extremely challenging and limiting, often with the use of "off label" adult devices. The Carpediem system was approved in the United States for extracorporeal CKST for infants weighing 2.5 to 10kg. The purpose of this case series is to describe a single center experience of patients treated with the Carpediem system.

Methods: A single center retrospective cohort of neonatal CKST performed with the Carpediem system between June 1, 2021, and November 30, 2021. A retrospective chart review was performed including demographics, clinical and laboratory variables, and CKST characteristics.

Results: Seven (57% male; 71% delivered in-center) neonates received CKST with 015 (67%) or 025 (17%) hemofilter in the neonatal (71%) and cardiac intensive care units (29%). Median fluid overload was 23% (Interquartile range [IQR] 16.5-33.5) at initiation. Most were preterm, 29% extremely low gestational age (<28 weeks), 43% preterm (32-35 weeks), and 14% late preterm (35-37 weeks); 29% were extremely low birth weight (<1000g). 86% had congenital malformations (57% diagnosed prenatally) including 43% congenital anomalies of kidney and urinary tract (14% lower urinary tract obstruction, 29% renal dysplasia), 29% had seizures, and 29% had confirmed sepsis. Indication for CKST initiation was 57% fluid overload and 43% neonatal end stage kidney disease (ESKD). Prior to CKST start, 43% had intracranial hemorrhage and 29% had thrombi.

Initial vascular access was 8 Fr in 43%, 7.5 Fr in 43%, and 7 Fr in 14%. Median number of catheters per patient was 2 (IQR 1.25-2). Median prescribed blood flow was 6.3 ml/kg/min (IQR 5.9-9.1). All patients received continuous venovenous hemodialysis with a starting clearance of 2000 ml/1.73m2/h and regional citrate anticoagulation. Median effluent dose prescribed was 94.4 ml/kg/h (IQR 90.9-102.2). Median effluent urea to BUN ratio was 63.0% (IQR 62.4-63.8). Average circuit life was 17.5 hours (range 8.0-20.9). Adverse events included 14% catheter-associated thrombus and 14% central venous line-associated thrombus. 71% patients survived their CKST course and 57% successfully transitioned to peritoneal dialysis (PD), 14% currently receiving CKST.

Conclusion: CKST can be performed successfully, including in low birth weight neonates, with the Carpediem system. This platform allows successful support of neonatal ESKD before other modalities could be used such as PD.

Abstract Category: D) RRT Applications and Targeted Interventions

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Use of the Vexus Protocol (Evaluation of Venous Congestion with Sonographic Guidance) in the Adjustment of Dry Weight and its Correlation with Bioimpedance in Patients on Intermittent Hemodialysis

LUIS JOSE CABRERA MIRANDA[1], ANA KARINA GARCIA SAMANO[1], DIANA MALDONADO TAPIA[1], MONICA LOPEZ MENDEZ[1], JOSUE MEZA[1], MARIBEL SANTOSBEÑA LAGUNES[1], OSCAR LOPEZ SANTIAGO[1], CARLOS AGUILAR NIETO [1]

[1]*CENTRO MEDICO NACIONAL 20 DE NOVIEMBRE ISSSTE*

ABSTRACT: In November 2021 we performed pre-hemodialysis and post-hemodialysis vexus and bioimpedance measurements. In a total of 38 patients, bioimpedance measurements and taking were performed in the long and short interdialytic periods, a total of 304 sonographic measurements and 304 bioimpedances, sonographic measurements were carried out by expert personnel in medicine, critical medicine, critical echocardiography and nephrology. while the bioimpedances by nutrition personnel with a master's degree in clinical nutrition and nutrition in adult kidney patients. Primary objective of the study was to establish an association between vexus pattern and bioimpedance through statistical correlation to serve as an additional and even equally effective tool for adjusting dry weight in patients on intermittent hemodialysis, to guide fluid removal in this group of patients. patients. The secondary objectives were focused on diuretic adjustment and use of antihypertensive drugs.

METHODS A total of 38 patients were enrolled in this study with diagnoses of chronic kidney disease of different etiology, belonging to the hemodialysis unit of the National Medical Center November 20 of the ISSSTE in Mexico City, with obtaining informed consent they were divided into 2 groups for measurements in week 1 and week 2, vexus and bioimpedance were performed in the long and short interdialytic periods, for the pre hemodialysis measurement 30 minutes prior to connection was taken into consideration and for the post hemodialysis period it was considered 1 to 2 hours After disconnection, bioimpedance and mamometry were taken in parallel, a Siemens Healthineers ultrasound equipment was used, with the use of a 2.5 to 5 MHz transducer and a 2 to 5 MHz transducer, the vexus parameters were maximum, minimum and minimum diameters. vena cava collapse, the pattern of the hepatic vein and the analysis and measurement of the portal vein pulsatile index were analyzed. Long pre-dialytic period results: maximum vena cava diameter vs phase angle: spearman's rho 0.469. % collapsibility vs total body water in stones: spearman's rho 0.549. Maximum vena cava diameter vs intracellular water: spearman's rho -0.493. Minimal vena cava diameter vs intracellular water: spearman's rho -0.567. % collapsibility vs phase angle: spearman's rho 0.743. short pre-dialytic period: pro bnp vs phase angle: spearman's rho -0.593

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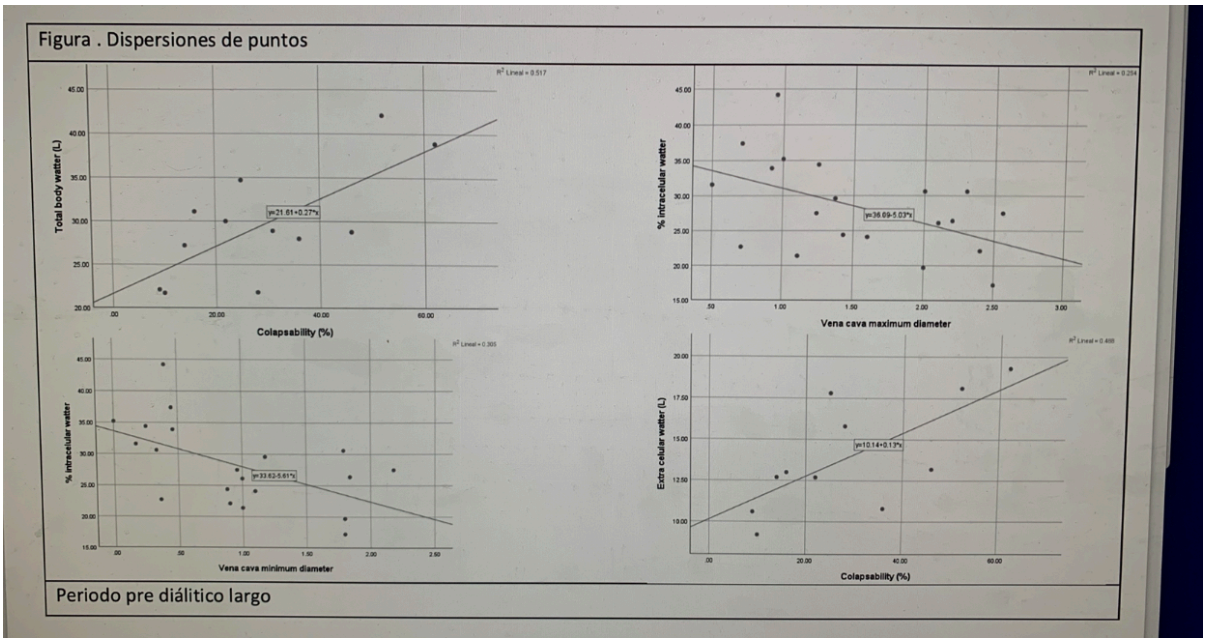

Abstract Category: D) RRT Applications and Targeted Interventions

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Improving awareness of kidney function through electronic urine output monitoring: a comparative study

Daniel Fernando Orjuela Cruz[1], Omar L Murad[1], Aliza Goldman[2], Peter Vernon Van Heerdan[1]

[1]*Hadassah Medical Center,* [2]*Renalsense Ltd.*

Introduction: Intensive monitoring of a patient's vital signs and physiological parameters in the intensive care unit (ICU) provides timely information and enables rapid response by the attending medical staff. The KDIGO (Kidney Disease Improving Global Outcomes) guidelines suggest a 'bundle' approach for treating patients that are at risk of developing acute kidney injury (AKI). This bundle includes, along with other monitoring, maintenance of volume status and monitoring of serum creatinine (SCr) and urine output (UO). One of the few remaining parameters monitored manually in the ICU is UO.

Methods: From December 2019 through November 2020 RenalSense Clarity RMS Consoles were installed on every bed in the General Intensive Care Unit (GICU) in the Hadassah Medical Center, Israel. Along with its Sensor Kit (including drainage bag connecting to a standard Foley catheter), the system continuously monitors UO in real-time. One hundred patients were randomly selected from this period as the study group (UOreal-time). Patient data was compared to a matched control group (UOmanual) from December 2017 through November 2018. Urine output, as well as administration of fluid bolus and diuretics, were analyzed for the first 48 hours of hospitalization. Oliguric hours were defined as UO below 0.5ml/kg/hr.

Results: The study group (UOreal-time) showed a significant correlation of patient oliguric hours and treatment with furosemide or fluid bolus, while the matched control group (UOmanual), showed no such correlation. (p-value = 0.017, and 0.932, respectively).

Conclusion: The results strongly suggest that the use of electronic urine monitoring contributed to meaningful medical intervention. Other studies have shown that close monitoring of UO and patient fluid status, is central to identify those at risk of developing AKI. Real-time electronic UO monitoring can promote earlier intervention and better application of goal-directed patient treatment.

Abstract Category: E) New Technology

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In Vitro Clearance Performance of the Manual Single Lumen Alternating Micro-Batch (mSLAMB) - Potential Use in Austere Medical Environments

Apaara K Chawla[1], Denise C Hasson[2], Jolyn R Morgan[2], James E Rose[2], Stuart L Goldstein[2]

[1]*Francis Parker Upper School, San Diego, CA,* [2]*Center for Acute Care Nephrology, Cincinnati Children's Medical Center*

Introduction: Most blood based renal replacement therapies (RRT) use a double lumen access to create a circuit to dialyze blood. A single lumen alternating micro-batch (SLAMB) has been developed that uses a single lumen to perform RRT. A variation of this single-lumen system is the manual SLAMB-HF (mSLAMB) kit. The mSLAMB works without need for electricity, a battery, or a pump thus making it useful for medical situations in austere environments. The mSLAMB uses syringes, gravity, and standard intravenous fluids to effect RRT.

Methods: In vitro clearance experiments were conducted with the mSLAMB. The mSLAMB was connected to a 2-liter bag of a mixture of expired human packed red blood cells and 0.9% NaCl to achieve a hematocrit of approximately 35%, which was spiked with urea resulting in a blood urea nitrogen concentration of 50 - 120 mg/dL and potassium levels of 9.9-16.6 meq/L. Three sets of experiments were conducted, each with a different ratio of hemofiltration fluid to blood volume. Three different dialyzers were also tested. The first set was hemofiltration series in a one-to-one ratio, with 100 cc of blood and 100 cc of hemofiltration fluid pulled. This was repeated, and the second and third experiments had a one-to-two ratio and a one-to-three ratio respectively. Eight cycles were performed in each set, and reduction of urea and potassium concentrations were recorded. The data were normalized by percent removed.

Results: The aggregate results present a urea reduction ratio (URR) of 27.4 + 7.1% after 8 cycles. The predicted URR was 20.9 + 3.2% (Figure 1). Mean percentage reduction of potassium was 23.4 + 9.3%. The mean URR for at the end of each cycle are shown in Figure 1. The mean potassium reduction for cycles 1-8 were: (1) 11.4[4.9]%,(2)12.8[9.5]%,(3)16.5[5.4]%,(4)17.2[6.7]%,(5)20.0[6.0]%,(6)22.5[8.8]%, (7)23.0[7.5]%,(8)23.4[9.3]%. The largest reduction percentage for both urea and potassium occurred after the first cycle.

Discussion:The mSLAMB disposable system removes urea and potassium effectively. The efficiency of the mSLAMB was similar across three different sizes of dialysis filter and membrane type. Since the mSLAMB only requires manual syringe labor and gravity, this device allows healthcare workers to offer dialysis in austere medical conditions or environments with limited resources. This creates a potential availability of dialysis services worldwide allowing medical professionals to treat people where they could not before.

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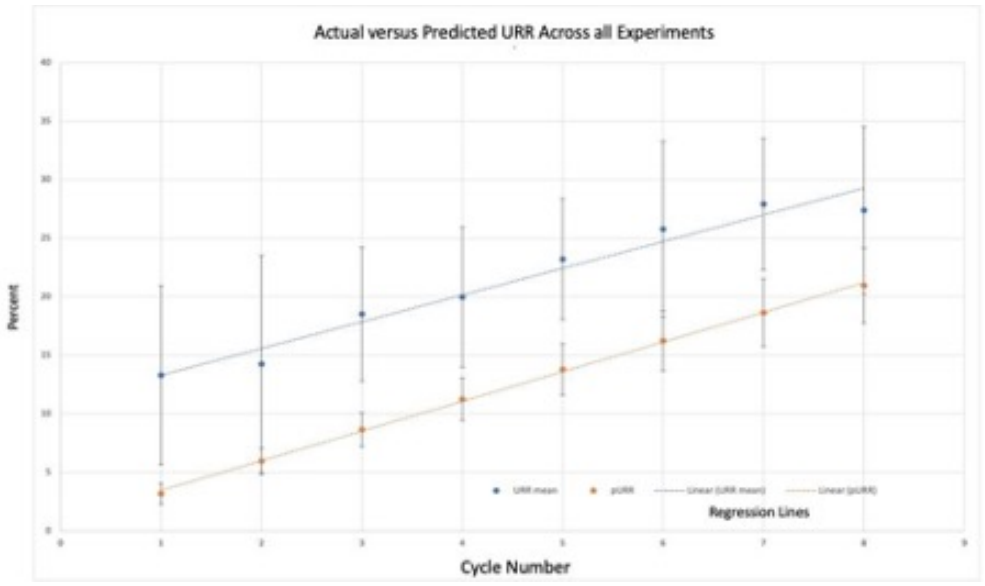

Abstract Category: E) New Technology

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Blood Flow Rates and Ultrafiltration Accuracy in a Manual Single Lumen Alternating Micro-Batch Dialysis Circuit

Denise C Hasson[1], Apaara K Chawla[2], Jolyn R Morgan[1], James E Rose[1], Ellen M Cody[1], Stuart L Goldstein[1]

[1]*Cincinnati Children's Hospital Medical Center,* [2]*Francis Parker School, San Diego, CA, USA*

Purpose: Electrolyte derangements and volume overload remain life threatening emergencies in low resource settings. The manual Single Lumen Alternating Micro-Batch (mSLAMB) dialysis system is envisioned to treat severe acute kidney injury (AKI) and its sequelae when a standard dialysis machine or peritoneal dialysis are not available. Blood is drawn in small batches from the patient into a sterile tubing circuit, and a hemofilter provides a diffusive surface for clearance, while syringes can pull fluid off for ultrafiltration. Through this closed loop system, we believe clearance and volume removal is not only possible, but efficient and volumetrically accurate. We sought to determine blood flow rates (Qb) and ultrafiltration accuracy using mSLAMB to dialyze human blood in vitro.

Methods: We used units of expired packed red blood cells diluted with 0.9% NaCl to a final hematocrit of 30-35% and anticoagulated with heparin to simulate the pediatric patient blood volume. The duration of each cycle was timed to determine Qb, using a 2x2 factorial design to assess the effect of the height difference between reservoirs and volume on Qb. Differences in height between reservoirs (35cm vs 45cm) and crystalloid hemofiltration fluid volumes (aliquots of 50mL of blood added to either 50mL or 150mL of crystalloid) were tested. Student's T-test was used to compare groups. Effluent volumes were recorded after each run and compared to prescribed volume to assess ultrafiltration accuracy.

Results: 6 runs of 8 cycles each were time recorded. Mean (+/- SD) Qb of the 100mL vs. 200mL volume group was 80.3 +/- 5.1 vs 90.2 +/- 7.0 mL/min (p=0.03). Mean (+/- SD) Qb of the 35cm vs. 45cm height difference was 79.7 +/- 4.4 vs 90.8 +/- 6.5 mL/min (p=0.01). Higher volume and greater height difference improved Qb (Figure). Mean difference between volume prescribed and measured was 11.4mL for prescription volumes of 800-2400mL. Percent absolute difference between volume prescribed and measured ranged from 0 to 2.4% and did not increase with increasing volumes.

Conclusion: We consistently and precisely achieved blood flow rates comparable to an automated continuous dialysis machine with accurate ultrafiltration volume. Increasing height between reservoirs and volume dialyzed synergistically improved Qb without sacrificing ultrafiltration accuracy.

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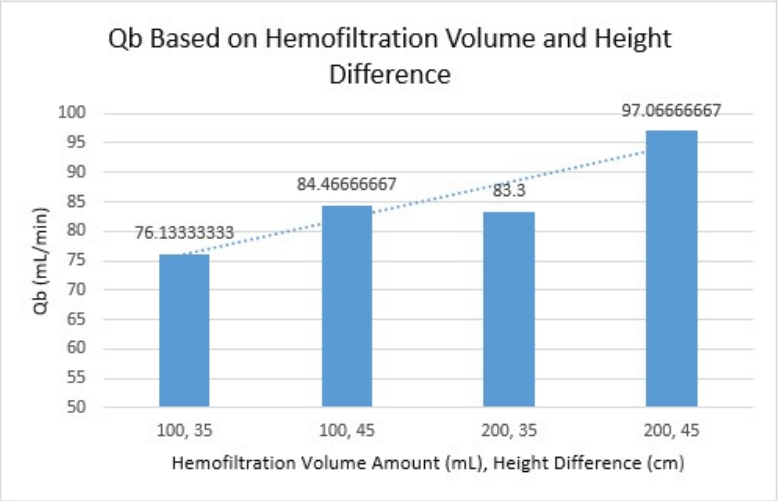

Figure legend: Blood flow rates based on hemofiltration volume and height difference, 2-way ANOVA p=0.11. Qb-blood flow rate.

Abstract Category: E) New Technology

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Coupled Plasmafiltration Adsorption As a Effective Blood Purification Method To Remove Albumin-Bound Toxins in Acute On Chronic Liver Failure.

Rafael Avila [1], Yamila Lombi [1], Ezequiel Manrique[1], Martin Barrabino[1], Martin Maraschio[1], Damian Conte [1], Jesica Rechene [1], Virginia Mir [1], Enzo Giordano [1]

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Artificial extracorporeal liver support devices (ECLS) aim to remove albumin-bound and water-soluble toxins to restore and preserve liver function mitigating the progression to multi-organ failure during liver recovery or until liver transplantation. Coupled plasma filtration adsorption (CPFA) system consists of plasma separation followed by plasma adsorption through a resin cartridge with high affinity for bilirubin , bile acids, tryptophan and phenols.We evaluate the capacity of this technique to detox liver toxins.

Data from 5 patients with acute on chronic liver failure (AoCLF) underwent CPFA were collected.

The treatment was carried out using the Amplya machine (Bellco), through a temporary femoral catheter 13,5 French ; Sodium heparin in continuous infusion of 5-10 IU / kg or citrate was applied as anticoagulant according to our protocol. The plasma exchange was set up automatically from 13 to 20% of the blood flow.

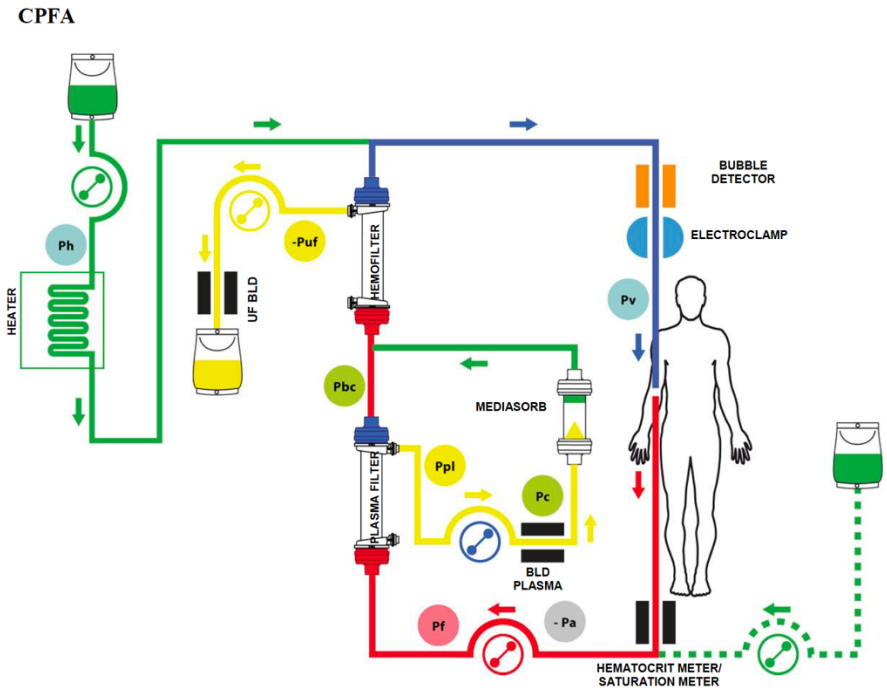
The criteria to start CPFA were ACLF that did not respond to the usual medical treatment, a rise in serum bilirubin rapidly of more than 50% with respect to the value of ICU admission or MELD score> 20 before performing the liver transplant.
Causes of liver failure: autoimmune origin 2, alcoholic hepatitis 1 and loss of liver graft in previously transplanted patients 2.

The patients mean age was 42 (21- 67), mean MELD 21 (36-23), mean
SOFA score 9 (7-11). All patients received 1 session of CPFA except one 2 sessions. Plasma processed dose (0,16L/kg/session), session duration 6 (h).The procedure was hemodynamically well tolerated, without the need for the use of vasopressors. In all cases, a decrease in the plasma level of total bilirubin, direct bilirubin, biliary acid of 31%,33% and 28% were evidenced.

Our study shows the high effectiveness of CPFA removing albumin-bound toxins. Furthermore, the new generation of machines make it easier to combine diffusion, convection and adsorption. Altogether allows to remove a wide range de solutes of different molecular weigh
To date, this type of treatment is an option as a bridge to transplantation or recovery.

CPFA is a treatment that improves the metabolic condition of patients with cirrhosis , allowing them to reach the transplant in better conditions. The main advantage is its ability to treat high

volumes of plasma without the need for albumin replacement, which makes it potentially inexpensive and of short duration without generating hemodynamic intolerance.



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Conductivity Meter as a Novel Device for Real-Time Urinary Electrolyte Monitoring

Ami Mayo[1], Avishai Manos[2], Itzik Barnett[1], Aliza Goldman[2], Tamar Bar - Nur[2], Hagar Azran[2]

[1]*Assuta Hospital, Ashdod, Israel,* [2]*RenalSense, Jerusalem, Israel*

PURPOSE: Although Acute Kidney Injury (AKI) identification and classification have improved over the years, online methods to distinguish between renal AKI and prerenal AKI are still missing. Considering the consequences of misdiagnosis and mistreatment of different types of AKI, a reliable online monitoring system that enables assessment of the kidney's ability to concentrate or dilute urine in response to injury and treatment is critical. RenalSense has developed a novel urine real-time conductivity monitoring system that monitors the concentration of urine electrolytes, integrated with Urine Output (UO) measurements. The objective of this study was to establish the reliability and accuracy of the urine conductivity monitoring device.

METHODS: Throughout the preclinical phase, in vitro tests were performed to examine the safety, uniformity, consistency, reliability, and quality of the urine conductivity monitoring system. In the clinical trial phase, a validation procedure was performed by extracting urine samples from the patients' sample ports. The urine samples were tested for conductivity, electrolytes, and urinalysis in the laboratory. The laboratory measurements were compared to those measured by the novel system in clinical trials. The correlation between the concentration of urine electrolytes to measured conductivity values was also tested.

RESULTS: Twenty-five ICU patients were enrolled in the clinical study. A high correlation was found between lab conductivity measurements to those conducted by the novel conductivity monitoring system. As expected, the results showed a correlation between urine electrolyte concentration to conductivity, confirming that conductivity values reflect the urine electrolyte concentration.

CONCLUSIONS: Although the establishment of KDIGO (Kidney Disease Improving Global Outcomes) criteria and the clinical use of automatic devices for UO measurements have advanced the diagnosis of AKI, a reliable tool for AKI classification is still lacking. The conductivity monitoring system was tested and found to be reliable, safe, accurate, and consistent. Our study shows that real-time measurements of urine electrolytes can provide valuable insight into a wide range of clinical conditions.

Abstract Category: E) New Technology

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Real-Time Urinary Electrolyte Monitoring as a Novel Clinical Tool for Diuretic Responsiveness Assessment

Ami Mayo[1], Avishai Manos[2], Itzik Barnett[1], Aliza Goldman[2], Doron Levin[2], Hagar Azran[2]

[1]*Assuta Hospital, Ashdod, Israel,* [2]*RenalSense, Jerusalem, Israel*

PURPOSE: The term "urine electrolytes" is generally used to indicate urine concentrations of sodium, potassium, and chloride excreted by the kidneys. Those values reflect the balance between glomerular filtration, tubular secretion, and reabsorption of water and solutes, which can vary significantly under different pathophysiological and treatment conditions. While diuretics are used in approximately half of ICU admissions, their efficacy remains unclear. Administration of low-dose furosemide modifies urinary electrolyte excretion rates, in relation to the ongoing proximal tubular activity, by its inhibitory action on Henle's loop. Therefore, monitoring the concentration of urinary electrolytes would indicate the furosemide impact, and will provide a new and rapid method for testing its efficacy. RenalSense has developed a novel urine conductivity monitoring system that continuously monitors the concentration of urine electrolytes in real-time, along with Urine Output (UO). The aim of this study was to evaluate how urine conductivity monitoring can assess diuretic responsiveness.

METHODS: The conductivity monitoring system was connected to 24 patients admitted to the Assuta Ashdod ICU. UO and electrolyte measurements were continuously recorded, before and after diuretic administration. Fourteen patients received diuretics, for a cumulative total of 41 days. In 51% of the days, the patients received bolus furosemide, whereas in 49% of the days, patients received a continuous IV drip of furosemide or metolazone.

RESULTS: Twenty-one days of bolus furosemide administration were analyzed. In 17 out of the 21 days, urine electrolyte elevation was seen immediately after the furosemide administration, followed by a UO increase. However, in four cases, there was a decrease in the urine electrolyte level, followed by a decrease of UO. The diuretic impact on the urine electrolyte level is immediate and therefore can predict the urine output diuretic response even within minutes.

CONCLUSIONS: The conductivity monitoring system provides a new tool for fluid management and diuretic use response. Continuous real-time measurements of urine electrolytes also improve Acute Kidney Injury (AKI) classification and can assist in tailoring patient diuretic and hemodynamic therapies. Further clinical trials are required to establish the correlation between urine electrolyte level and diuretic responsiveness.

Abstract Category: E) New Technology

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Insights into serum metabolic biomarkers for early detection of incident diabetic kidney disease in patients with type 2 diabetes by random forest

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Aims: Diabetic kidney disease (DKD) is the most common cause of end stage renal disease (ESRD). Given the paucity of metabolic studies on DKD in patients with type 2 diabetes mellitus (T2D), we aimed to characterize its features of untargeted metabolites and identify candidate metabolic biomarkers for its early detection.

Methods: Untargeted metabolites by UPLC-Orbitrap-MS was performed on serum of 194 Chinese adults include 164 T2D patients and 30 healthy participants. We only retained MS-detected compounds that correlated with estimated glomerular filtration rate (eGFR) (Spearman's $r \geq 0.4$) for further analysis. To identify candidate DKD progression related biomarkers (CDBs), we evaluate the correlation among metabolites and multiple clinincal parameters such as estimated glomerular filtration rate (eGFR), urinary albumin-to-creatinine ratio (UACR), serum creatinine (sCr), urinary β2-microglobulin, renal resistive index (RRI) and body surface-area related renal volume (BSA-RRV). The closely correlated metabolites were subjected to random forest (RF) analysis to assess their predictive power. The selected CDBs were further tested in 106 follow-up patients during averagely 3.9 years by calculating the area under the cure (AUC) of their receiver operating characteristic curves (ROC).

Results: A total of 17528 compounds were detected. After a stringent filtering pipeline, pseudouridine, L-TMAP, 2-(α-D-mannopyranosyl)-L-tryptophan (AD-trp) and succinyladenosine (S-Ado) were found to strongly associate with the development of DKD and were regarded as CDBs. RF analysis showed that their levels can differentiate the stages of patients in consist with eGFR. Any one of the CDBs combined with MS-detected creatinine (MS-Cr) achieve better performance than MS-Cr alone in DKD staging. The combination of "MS-Cr + pseudouridine + L,L-TMAP" ranks the best in phasing the very early stage ($eGFR \geq 120$) with average $AUC > 0.9$. In the follow-up study, we found the level of three CDBs include AD-trp, S-Ado and pseudouridine have good potential in predicting the DKD progression with average $AUC > 0.7$. For patients at early stage ($60 \leq eGFR \leq 90$), UACR combined with AD-tryp (average $AUC = 0.942$) can significantly improve the predictive power of UACR alone (average $AUC = 0.860$).

Conclusion: Our results showed these CDBs are promising to support phasing and/or predicting the early DKD and have the potential to be utilized in future clinical trial.

Abstract Category: E) New Technology

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Set-up and Perform Dialysis Using the Manual Single Lumen Alternating Micro-Batch Hemodiafiltration (mSLAMB) System

Jolyn Morgan [1], Denise Hasson [1], Apaara Chawla [2], James Rose [1], Stuart Goldstein [1]

[1]*Cincinnati Children's Hospital Medical Center ,* [2]*Francis Parker Upper School, San Diego, CA*

Purpose: The mSLAMB system is a novel sterile and closed-loop dialysis system designed to provide kidney support in emergency situations (e.g., fluid overload, hyperkalemia, acidemia) where dialysis machines, peritoneal dialysis, and/or electricity are unavailable. mSLAMB circuits costs <$50. We conducted in vitro experiments to determine the best training method, ease of set-up, and efficiency.

Methods: We describe supplies, set-up, and a single cycle of the mSLAMB procedure. Supplies: 1- disposable kit, 2- IV poles, 1 Liter prime solution (PS), Hemofiltration fluid (HF), 1 filter, 1 filter holder; 2- 50 mL syringes, 1- graduated cylinder, 2- hemostats. Set-up: staircase 2 IV poles (#1 closest to patient (pt) and higher than #2); hang PS on IV #1; hang HF bag and blood reservoir (BR) #1 bag to right of PS & attach 50 mL syringe to right of HF stopcock (SC); attach filter holder & filter to IV #2 & attach red luer lock from BR #1 to filter inlet; hang BR #2 on IV #2 & attach red luer lock to filter outlet; attach Hansen connector to one side of the filter & attach 50 mL syringe to SC; spike PS bag & begin gravity prime; discard PS. Procedure: attach bloodline to access & turn SC off to pt; open HF bag SC, pull 50 mL's & push plunger to fill BR #1; turn SC off to HF bag & open pt SC, pull 50 mL's of blood and push plunger to fill BR #1; close white clamp before BR #1 and begin dialysis (blood moves from BR #1 to filter to BR #2), pull 50 mL's of HF fluid from UF SC (increase removal to achieve negative fluid balance); raise BR #2 higher than BR #1 and gravity drain back to BR #1; begin pull/push to return dialyzed blood to pt.

Summary: mSLAMB procedural training was accomplished in 1 day. Instructional videos will be provided and a "training the trainer" approach will build a group of competent users who can teach others. mSLAMB can be prepared and ready for use in ~10 minutes. The procedure is easier using small batches (50- 100 mL) of blood and more efficient with 2 people but can be performed by 1 person.

Conclusion: mSLAMB is a simple, cost effective, and potentially life-saving alternative for low resource settings. Treatment requires good single lumen access (e.g., IV) but does not require a pump or special dialysis solution. Any sterile balanced solution (e.g., LR) will allow provision of sufficient dialysis until the patient can be relocated/ transferred.

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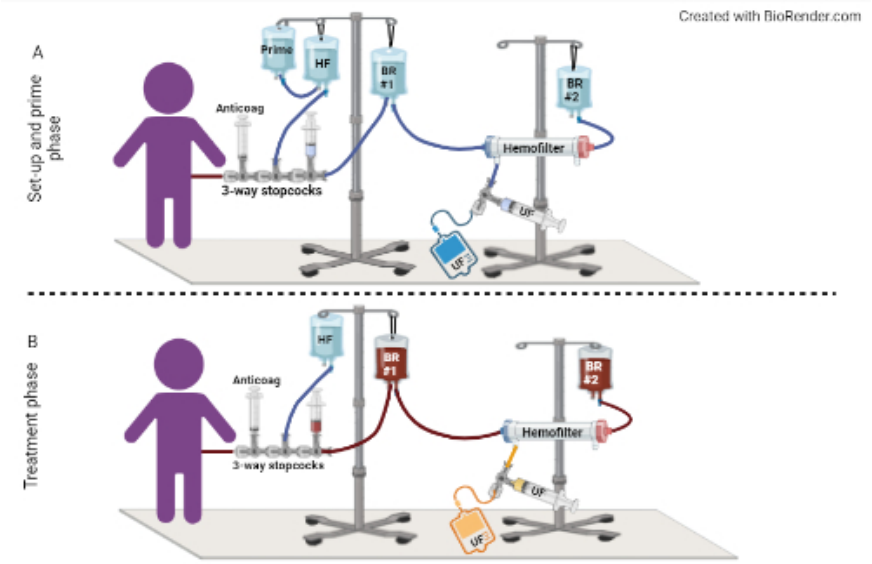

Figure 1. A. mSLAMB set-up and prime phase [hemofiltration fluid (HF), blood reservoir (BR), ultrafiltration (UF); B. Treatment phase

Abstract Category: E) New Technology

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In Vitro Simulation of Transdermal GFR Monitoring for Diagnosis and Theragnosis in a Patient with AKI

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[1]*MediBeacon Inc.,* [2]*Cincinnati Children's Hospital*

Background / Purpose:
We previously employed the MediBeacon Transdermal GFR Measurement System with our novel fluorescent tracer agent MB-102 to assess real-time CRRT clearance in nephrectomized pigs. Protocolized changes to blood pump and effluent flow rates were easily reflected in real time changes of MB-102 clearance detected by the transdermal fluorescent intensity measurements with time. These data showed almost an instantaneous jump from one clearance rate to another when the blood pump and effluent flow rates were changed.

To further explore how the MediBeacon Transdermal GFR Measurement System may perform in patients with AKI, an in vitro flow cell was constructed to mimic the depletion of MB-102 from the body under adjustable conditions.

Methods: The in vitro flow cell pumps a mixture of MB-102 dissolved in PBS, intralipid, and ink through a cuvette to which the sensor portion (light source and light detector) of the transdermal system is attached. The intralipid concentration mimics tissue optical scattering properties and the ink concentration mimics optical absorption due to skin color variations in the human population. The pumps of the in vitro flow cell are computer controlled with programs for specific GFR. Faster pump rates (rapid depletion of MB-102) mimic normal GFR, and slower pump rates mimic impaired GFR. This enables simulation of a dynamic GFR for which the response of the transdermal fluorescence instrumentation and its data processing algorithms may be observed and measured.

Summary of Results: The in vitro flow cell was programmed to simulate a patient with a normal GFR, followed by a lower GFR associated with an AKI event, then followed by return to the normal GFR to simulate a therapeutic intervention (e.g., fluid resuscitation or vasoactive medication initiation to improve renal perfusion). This sequence is shown in the Figure. The transdermal fluorescence detection system precisely mimicked the flow cell program, first measuring a normal clearance rate, then a resulting lower clearance rate with AKI, and then returning to the original clearance rate after intervention.

Conclusion: The dynamic capability of the MediBeacon Transdermal GFR Measurement System to monitor clearance and observe changes due to simulated kidney insult and/or intervention has been demonstrated in an in vitro model.

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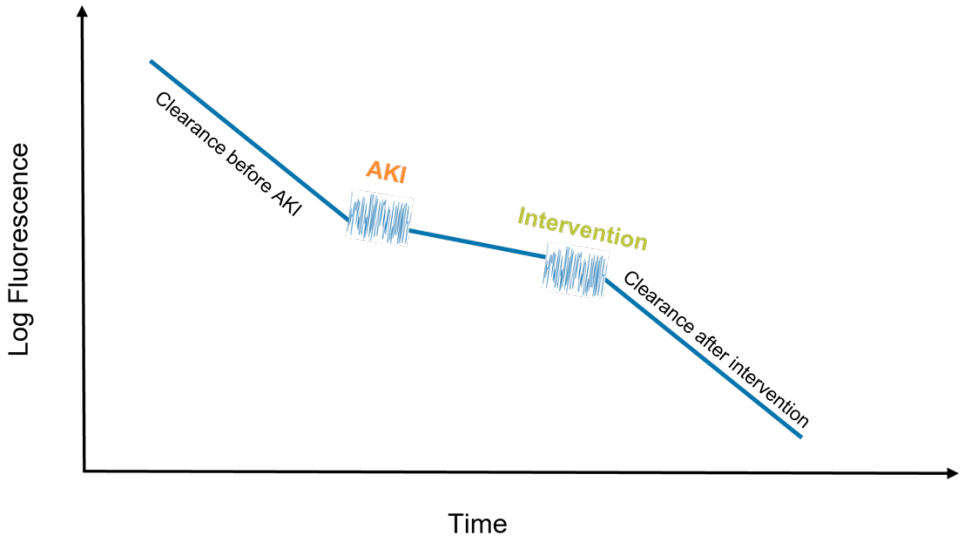


Abstract Category: E) New Technology

79

Automated diagnosis of acid-base disturbances

Innas Forsal[1], Mikael Bodelsson[2], Anders Wieslander[1], Anders Nilsson[1], Dominique Pouchoulin[1], Marcus Broman[2]

[1]*Baxter,* [2]*Skåne University Hospital Perioperative and Intensive Care*

Background/Aims
Acid base status is important for understanding pathophysiology, diagnosis, planning effective treatment and monitoring progress of critically ill patients in the intensive care unit (ICU). To do calculations manually is cumbersome and results easily in wrong conclusions. We developed a computer script that can diagnose acid base disorders and give both a numerical and a graphic diagnosis.

Methods
Acid-base understanding was combined with MATLAB computer programming, which resulted in a simplified adaptive computer script.
The script was used on 8875 patients' initial blood gases, drawn immediately after admission to the ICU.

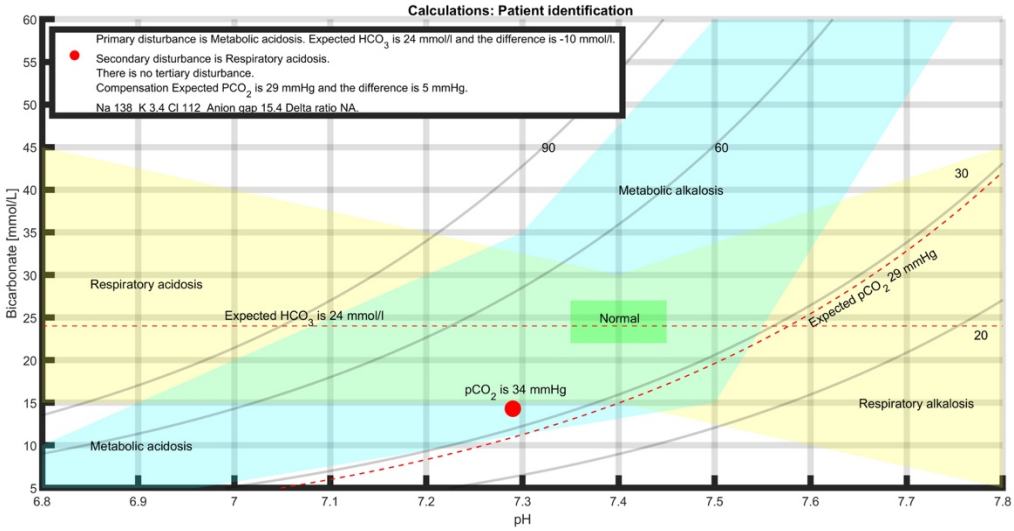
Results
In the cohort; 47% had no disturbance, 30% respiratory acidosis, 5% metabolic acidosis, 17% respiratory alkalosis and 1% metabolic alkalosis.
Both acute and chronic respiratory acidoses were significantly less compensated 78.4±17.3% and 87.1±9.9%, compared to acute and chronic respiratory alkaloses 91.1±6.3% and 92.7±5.8% ($p< 0.001$) respectively.
Metabolic acidoses were also significantly less compensated 63.0±6.4% compared to metabolic alkaloses 94.5±4.4% ($p<0.001$).
Our script worked well and presented a reasonable output for all blood gases calculated. It took 30.3 seconds to calculate all the 8875 blood gases (4437500 calculations) in comparison to a physician that requires 2-5 minutes to calculate one.

The graphic output is shown in Figure 1. The script draws a graph where pH is on the x-axis and bicarbonate level is on the y-axis. A superficial layer consisting of pCO2 isopleths is placed on top of the graph. The blood gas itself is represented by a red dot. The normal level, from which the primary disturbance has deviated, is drawn as a dotted red line. The expected level for full compensation is also drawn as a dotted red line.

Conclusion
The script could diagnose a single acid-base disturbance as well as calculate a huge cohort. The script can be installed on any software on any device or used as an app in a smartphone.

Figure on following page

Figure text
Figure 1 The acid-base diagnosis visualized. The blood gas is marked as a red dot. The patient has a metabolic acidosis (primary disturbance; bicarbonate 14 mmol/L and pH 7.29) and a respiratory acidosis (secondary disturbance; pCO2 is 34 mmHg when it should be 29 mmHg for full compensation).



Abstract Category: E) New Technology

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Impact of Serum Albumin on Mortality of Patients on Continuous Renal Replacement Therapy

Yeshwanter Radhakrishnan[1], Charat Thongprayoon[1], Wisit Cheungpasitporn[1], Fawad Qureshi[1], Michael A Mao[1], Kianoush B Kashani[1]

[1]*Mayo Clinic*

Background: Hypoalbuminemia (albumin ≤3.5 g/dL) at the time of admission has been shown to be associated with increased in-hospital mortality, length of hospital stay and re-admissions in non-critically ill patients1. This study aimed to assess the impact of hypoalbuminemia on mortality in critically ill patients requiring continuous renal replacement therapy (CRRT).

Methods: This is a retrospective cohort study of critically ill patients receiving CRRT for acute kidney injury from December 2006 through November 2015 in a tertiary referral hospital in the United States. Patients were excluded if they had history of end-stage kidney disease or received any dialysis modalities within 7 days before CRRT initiation, died within 24 hours of CRRT initiation and did not provide research authorization. We used logistic regression to assess serum albumin before CRRT as predictors for 90-day mortality. The normal reference range for serum albumin was 3.5-5.0 g/dL.

Results: A total of 911 patients requiring CRRT were included in this study. The mean serum albumin at CRRT initiation was 3.0±0.7 g/dL. The 90-day mortality was 57%. Serum albumin levels of ≤2.4, 2.5-2.9, 3.0-3.4, and ≥3.5 g/dL were noted in 24%, 29%, 24%, and 23% of patients, respectively. In adjusted analysis, serum albumin ≤2.4 g/dL was significantly associated with higher 90-day mortality with OR of 1.58 (95% CI 1.02-2.46), compared serum albumin ≥3.5 g/dL. Serum albumin 2.5-2.9, and 3.0-3.4 g/dL were not associated with mortality. Sensitivity analysis in patients requiring CRRT in setting of acute kidney injury showed consistent results

Conclusion: Approximately three out of four patients had hypoalbuminemia ≤3.4 g/dL at CRRT initiation. However, only severe hypoalbuminemia ≤2.5 g/dL was significantly associated with higher mortality.

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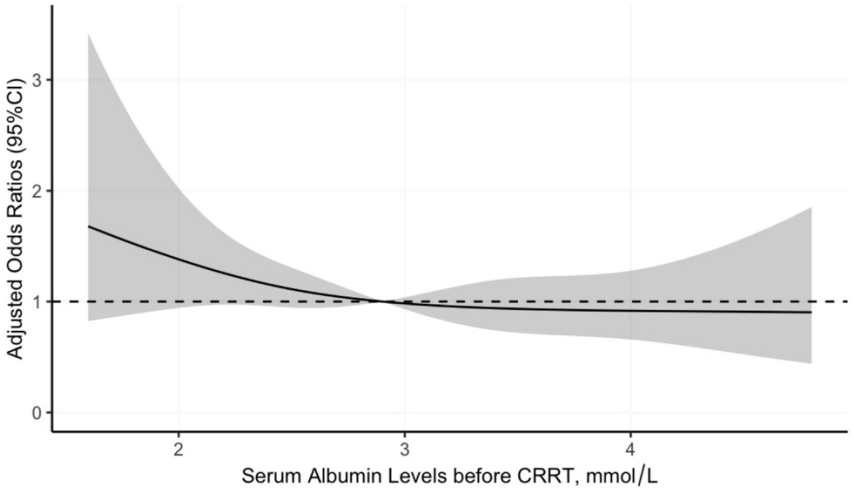

Abstract Category: F) RRT Research

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Association of Hypochloremia with Mortality among Patients Requiring Continuous Renal Replacement Therapy

Yeshwanter Radhakrishnan[1], Charat Thongprayoon[1], Wisit Cheungpasitporn[1], Jose L Zabala-Genovez[1], Michael A Mao[1], Kianoush B Kashani[1]

[1]*Mayo Clinic*

Background: Serum chloride derangement is common in critically ill patients requiring continuous renal replacement therapy (CRRT). We aimed to assess the association between serum chloride before and during CRRT with mortality.

Methods: This is a retrospective cohort study of critically ill patients receiving CRRT for acute kidney injury from December 2006 through November 2015 in a tertiary referral hospital in the United States. Patients were excluded if they had history of end-stage kidney disease or received any dialysis modalities within 7 days before CRRT initiation, died within 24 hours of CRRT initiation and did not provide research authorization. We used logistic regression to assess 1) serum chloride before CRRT, and 2) mean serum chloride during CRRT as predictors for 90-day mortality after CRRT initiation. The normal reference range for serum chloride was 99-108 mmol/L.

Results: Of 1,282 eligible patients, before CRRT initiation, 25%, 50%, and 25% had hypochloremia, normochloremia, and hyperchloremia, respectively. The adjusted odds ratio for 90-day mortality in patients with hypochloremia before CRRT was 1.83 (95 %CI 1.30-2.56). During CRRT, 4%, 70%, 26% of patients had mean serum chloride in hypochloremia, normochloremia, and hyperchloremia range, respectively. The adjusted odds ratio for 90-day mortality in patients with mean serum chloride during CRRT in the hypochloremia range was 2.95 (95% CI 1.43-6.10). Hyperchloremia before and during CRRT was not associated with mortality.

Conclusion: Hypochloremia, but not hyperchloremia, before and during CRRT was associated with higher mortality.

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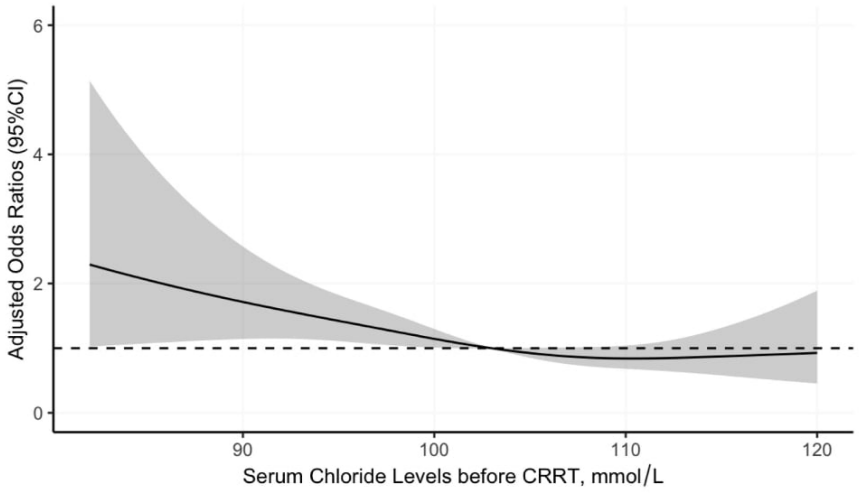
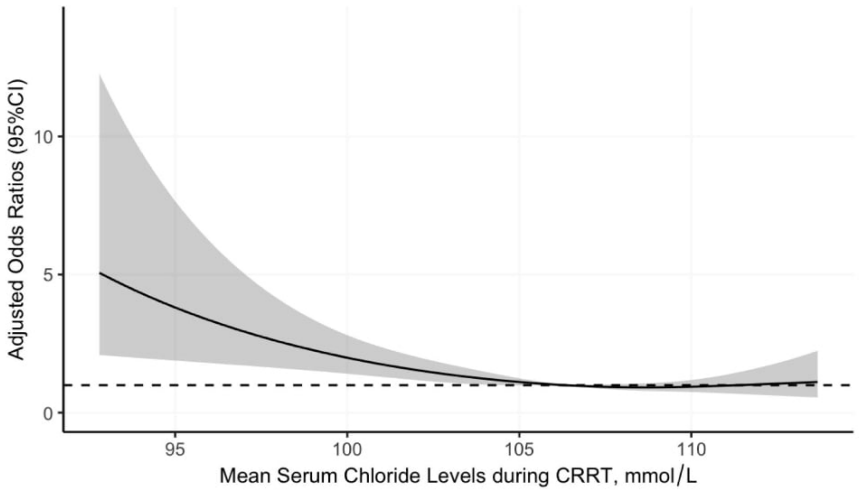

Adjusted Odds Ratios (95%CI)
6
4
2
0
90
100
110
120
Serum Chloride Levels before CRRT, mmol/L


Adjusted Odds Ratios (95%CI)
10
5
0
95
100
105
110
Mean Serum Chloride Levels during CRRT, mmol/L

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A Study of Dilution Modes under Different Operational Conditions in CVVH

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Introduction: An experimental study assessing specifically the effect of dilution modes on effective solute clearance in CRRT was investigated under CVVH mode, with pure post-dilution as the reference mode. The clearances for both small and middle molecules were measured for varying degrees of post/pre-dilution balance and different flow conditions.

Materials and Methods: The Prismaflex (Baxter) machine was used to deliver replacement fluid at different dilution points [pre-blood pump dilution (PBP), PRE and POST]. Simulated treatment (N=3 for each condition) involved 6 l of bovine blood (Hct ~ 35%, 34oC-36oC) processed at zero net ultrafiltration for a duration of 240 minutes. A 1.4 m2 hemofilter (HF 1400; Baxter) was used. The three experimental conditions were: 1) blood flow rate (QB): 190 mL/min; replacement flow rate (QR): 2 L/hr (33 mL/min), 2) QB: 290 mL/min; QR: ~3 L/hr (50 mL/min, 3) QB: 380 mL/min; QR: ~4 L/hr (67 mL/min). These conditions were chosen to maintain filtration > 25% in POST. Solute clearance estimates at various time points were based on mass balance calculations.

Results and Discussion: There were significant differences ($p < 0.001$) in urea and creatinine clearance for the different experimental conditions. There was a significant decrease ($p < 0.01$) in urea and vancomycin clearance from POST to PRE and from POST to PBP, although there were no significant differences between PRE and PBP for any of the solutes. There were significant differences ($p < 0.001$) in inulin and vancomycin clearance in these 3 experimental conditions. No significant differences ($p > 0.05$) in inulin clearance between post-dilution and pre-dilution mode, post-dilution and pre-pump-dilution mode, and pre-dilution and pre-pump-dilution mode were observed.

Conclusions: 1) SM solute clearance increased as the extent of Pre decreased 2) MM SC decreased substantially (especially in POST) with time, likely due to secondary membrane effects. 3) The data obtained by varying Pre- and Post percentages are predictable for SM but are not entirely consistent for MM. 4) Higher clearance values for MM can be achieved in Pre and PBP rather than in Post under low TMP. These results should be considered in the interpretation of recent CRRT dose/outcome studies.

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Kidney Support in Children using Aquadex: A Prospective and Retrospective Registry

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Purpose: Kidney Support therapy (KST) in small children can be technically challenging as machines designed for adult-sized patients necessitate large catheters and extracorporeal volumes. We sought to better characterize treatment with the Aquadex FlexFlow System (Nuwellis, Eden Prairie, MN) which is being used with increasing frequency in children with AKI, fluid overload, or congenital kidney failure (CKF).

Methods: We report preliminary demographic, therapy indication, and short- and long-term outcome data from this registry-based retrospective and prospective multi-center cohort of children receiving KST with Aquadex. Patients were grouped according to weight (<5, 5–10, and >10 kg). We determined fluid balance (%FB) at KST as the difference between dry weight and weight at KST initiation.

Results: To date, we have enrolled 82 patients (80 retrospective, 2 prospective) at 6 institutions. Patient size ranged from <5kg (N=45), 5-10kg (N=12) and >10kg (N=25). Patients had a variety of indications for KST. Patients were treated mostly in ICUs (89%). Treatment patterns and outcomes varied by patient size. In patients <5 kg, the primary disease was more likely to be kidney related (40%) while other cohorts were more heterogenous (Table 1). Regardless of patient size, the most common indications for KST were AKI with fluid overload (49%), fluid overload alone (32%), and CKF (11%). Patients <5kg had higher %FB at initiation than 5-10 kg and >10kg (19 (5,33) vs. 13 (7,16) vs. 5 (2,25); P=0.04), lower survival to Aquadex therapy completion (61% vs. 92 vs. 95%; P=0.004), and lower survival to hospital discharge (51% vs. 75% vs. 86%; P=0.015).

Conclusions: We report preliminary data from an ultrafiltration device registry describing a range of therapies for children in a variety of clinical settings. KST survival and survival to hospital discharge were superior to those reported in previous US registries. Smaller patients were more likely to have higher fluid balance at initiation and worse outcomes. Further completion of this multicenter registry will aid in the understanding of treatment characteristics and outcomes in children on Aquadex.

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Table 1. Patient Characteristics

Characteristic	Overall Cohort (n=82)	Weight <5kg (n=45)	Weight 5-10kg (n=12)	Weight >10kg (n=25)
Age at first KRT	4 (0.5, 32) mo	24 (9, 60) d	8.5 (4.5, 14.5) mo	133 (59, 188) mo
Female	32 (39)	19 (42)	4 (33)	9 (36)
Primary Disease				
Kidney	24 (29)	18 (40)	2 (17)	4 (16)
Cardiac	18 (22)	11 (24)	3 (25)	4 (16)
Sepsis	6 (7)	2 (4)	1 (8)	3 (12)
BMT/Transplant	4 (5)	0	3 (25)	1 (4)
Other	30 (36)	14 (31)	3 (25)	13 (52)
Primary Indication				
Volume overload	26 (32)	10 (22)	4 (33)	12 (48)
AKI and volume overload	40 (49)	20 (44)	7 (58)	13 (52)
AKI and electrolytes	7 (9)	7 (16)	0	0
CKF	9 (11)	8 (18)	1 (9)	0
Patient treatment location				
PICU	29 (32)	10 (22)	7 (58)	12 (48)
NICU	27 (33)	26 (58)	1 (8)	0
CICU	15 (18)	7 (16)	3 (24)	5 (20)
Other ICU	2 (1)	2 (4)	0	0
HF Floor	9 (11)	0	1 (8)	8 (32)
Dry weight, kg	3.8 (2.6, 11.8)	2.8 (2.0, 3.4)	8.4 (7.5, 9.2)	27.0 (13.2, 56.5)
Weight at therapy initiation, kg	5.8 (3.3, 13.2)	3.6 (2.7, 4.4)	9.2 (7.5, 10.2)	43.3 (16.4, 58.2)
%FB at KST initiation	13 (2, 27)	19 (5, 33)	13 (7, 16)	5 (2, 24)
Days in ICU before KRT	6.3 (1.6, 23.1)	5.5 (1.7, 16.1)	11.8 (0.6, 38.8)	9.5 (1.3, 23.3)
Treatment course survival (N=75)	57 (76)	25 (61)	11 (92)	21 (95)
Hospital survival (N=75)	49 (65)	21 (51)	9 (75)	19 (86)
Kidney Outcomes among survivors (N=50)	22 (44)	10 (48)	6 (60)	6 (32)
Renal Recovery	28 (56)	11 (52)	4 (40)	13 (58)
Discharged on Ongoing Dialysis				

AKI, Acute Kidney Injury; BMT, Bone Marrow Transplant; CKF, Congenital Kidney Failure; FB, fluid balance; KST, Kidney Support Therapy; HF, heart failure; mo, months

Abstract Category: F) RRT Research

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Clinical significance of serum albumin monitoring during continuous renal replacement therapy

Harin Rhee[1], Gum Sook Jang[1], Kyung Suk Jeong[1]

[1]*Pusan National University*

Introduction
Low serum albumin at starting CRRT is a risk factor for worse patient outcomes. However, less is known about its changing pattern during CRRT on patient outcomes.

Method
This is a single-center retrospective study based on the consecutively collected data receiving CRRT in a 3rd affiliated hospital. We excluded patients with end-stage kidney disease on maintenance dialysis, received CRRT less than 72 hours, or stayed hospital longer than 50 days. We collected serum albumin at CRRT initiation (A1) and 72 hours thereafter(A3). Changes in serum albumin were calculated as A3 minus A1. In-hospital mortality was compared using a cox regression analysis adjusted with initial serum albumin level.

Results
A total of 366 patients' data were available. Patients were median age of 69(57-78) years, 64.5% male, and median BMI of 22.8(20.1, 25.6) kg/m2. Of the included patients, 37.3% had diabetes, and 6.3% had liver disease. During a median of 16 (7, 27) days of hospital admission, we operated CRRT median of 4(3, 6) days and observed 43.3% of in-hospital death. At CRRT initiation, a mean SOFA score was 9.9±3.8, and the mean serum albumin level was 3.08±0.72 g/dL. At 72 hours after CRRT, the mean serum albumin level was 2.83±0.51g/dL, which was decreased by 0.25±0.69 g/dL ($p<0.001$). In the Cox regression analysis adjusted with serum albumin level at CRRT initiation, each 1g/dL increase in serum albumin level within 72 hours of CRRT was associated with a 54% reduction of in-hospital mortality (HR 0.464(0.297, 0.727), $p<0.001$), which was still effective (HR 0.549 (0.317, 0.950), $p=0.032$) when adjusted with age, BMI, diabetes, liver cirrhosis, SOFA score, and CRRT dose (Table 1).

Conclusion and discussions.
In patients who received CRRT for more than three days, increasing serum albumin level within 72 hours of CRRT was associated with decreasing in-hospital mortality. Based on the assumption that short-term changes in serum albumin level are mainly affected by changes in volume status, changes in serum albumin within 72 hours of CRRT might be considered as a possible surrogate marker of an amount of volume control. Further study will be needed to discover this issue in critically ill patients receiving CRRT.

Table on following page

	HR (95% CI)	P-value
Changes in Serum albumin (1g/dL)		
+ Serum albumin at CRRT initiation	0.464(0.297, 0.727)	<0.001
+ Serum albumin at CRRT initiation, age	0.478 (0.303, 0.755)	0.002
+ Serum albumin at CRRT initiation, age, BMI	0.422(0.260, 0.683)	<0.001
+ Serum albumin at CRRT initiation, age, BMI, DM	0.436(0.268, 0.708)	<0.001
+ Serum albumin at CRRT initiation, age, BMI, DM, LC	0.441(0.270, 0.721)	0.001
+ Serum albumin at CRRT initiation, age, BMI, DM, LC, SOFA score	0.511(0.298, 0.878)	0.015
+ Serum albumin at CRRT initiation, age, BMI, DM, LC, SOFA score, delivered dose	0.549(0.317, 0.950)	0.032

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ICONIC: Improving CARPEDIEM Outcomes in Neonates and Infants through Collaboration

Cara Slagle[1], Katja Gist[1], Kelli Krallman[1], Jolyn Morgan[1], Shina Menon[2]

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

BACKGROUND
Neonates receiving Continuous Renal Replacement Therapy (CRRT) experience worse outcomes compared to older children and adults. Previous studies attribute technical challenges to the lack of dedicated CRRT devices designed for children <10 kg. The CArdio-REnal PEdiatric DIalysis Emergency Machine (CARPEDIEM) is a dedicated platform designed to provide CRRT in a safe manner and improve outcomes in neonates and young infants. We have created a multicenter quality improvement and research registry dedicated to identifying best practices and treatment strategies to improve outcomes in this population.

METHODS
The collaborative was established with seven sites that were the first to offer CARPEDIEM therapy in the United States. It comprises representation from nephrology, intensive care units (ICUs), (pediatric, cardiac, and neonatology), and nursing. Specific aims of the collaborative include describing variations in CRRT prescription and delivery in neonates and establishing a registry for use in quality improvement and benchmarking efforts. For initial analyses, some areas of interest are CRRT dosing, anticoagulation protocols, safety and long term follow up. Institutional Review Board approval was obtained with intent to enroll all patients receiving CARPEDIEM at all sites.

RESULTS
To date, 14 centers have now joined ICONIC. An initial survey to describe institutional CARPEDIEM care delivery models and educational practices, and a subject database have been created using Research Electronic Data Capture (REDCap) tools hosted at Cincinnati Children's Hospital Medical Center. Alternating monthly meetings between the ICONIC steering committee and overall collaborative include discussion on CARPEDIEM use, program organization, and educational strategies. They will continue to guide program development and implementation at various centers with a designated "Clinical Practice Excellence" presentation. As centers become more established, we will move into analyses of existing data for variation and identification of best practices, and for answering the initial research questions on infant CRRT.

Abstract Category: F) RRT Research

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Hemofiltration Using A PMMA Membrane Inhibited Complement Activation, Decreased sCD40-Ligand Serum Levels And Improved Renal Function in LPS-Induced Experimental Acute Kidney Injury

Vincenzo Cantaluppi[1], Alessandra Stasi[2], Rossana Franzin[2], Chiara Divella[2], Fabio Sallustio[2], Antonio Crovace[2], Giovanni B Pertosa[2], Loreto Gesualdo[2], Claudio Ronco[3], Giuseppe Castellano[4]

[1]*University of Piemonte Orientale (UPO), Novara, Italy,* [2]*University of Bari, Italy,* [3]*International Renal Research Institute Vicenza (IRRIV), Vicenza, Italy,* [4]*University of Milan, Italy*

Background: Sepsis is the leading cause of AKI in critically ill patients refractory to conventional therapy. AKI is associated with multiple organ dysfunction and increased risk of mortality. Aberrant activation of the complement cascade and the release of soluble mediators such as the costimulatory molecule sCD40-Ligand (sCD40L) may affect organ damage leading to a poor prognosis. Polymethylmethacrylate (PMMA) membrane is known to have high absorptive capacity and biocompatibility.

Study aim: to investigate the efficacy of PMMA membrane-based continuous veno-venous hemofiltration (CVVH) in modulating systemic and tissue complement activation and sCD40L serum levels in a swine model of LPS-induced AKI.

Methods: Domestic pigs of 60 Kg body weight were subjected to i.v. administration of 300 mcg/Kg LPS vs. saline: after 3 h from LPS infusion, animals underwent to PMMA-CVVH or polysulfone (PS)-CVVH. Renal deposition of terminal complement mediator C5b-9 and of Pentraxin-3 (PTX3) deposits were evaluated on biopsies, whereas systemic Complement activation ans sCD40L levels were assessed by ELISA. Gene expression profile was performed from peripheral blood mononuclear cells by microarrays and the results validated by qRT-PCR.

Results: Endotoxemic pigs presented oliguric AKI with increased tubulo-interstitial infiltrate, extensive collagen deposition and glomerular thrombi: local PTX-3/C5b-9 renal deposits and increased serum activation of classical and alternative Complement pathways were found in endotoxemic animals. PMMA-CVVH but not PS-CVVH significantly reduced tissue and systemic Complement activation limiting renal damage and fibrosis. By microarray analysis, we identified 711 and 913 differentially expressed genes with a fold change >2 in endotoxemic pigs vs. PMMA-CVVH treated-animals. The most modulated genes were Granzyme B, Complement Factor B, Complement Component 4 Binding Protein Alpha, IL-12, SERPINB-1 ans sCD40L that were closely related to sepsis-induced immunological alterations. Mass removal studies confirmed the higher removal of sCD40L with PMMA-CVVH in respect to PS-CVVH.

Conclusion: PMMA-based CVVH can efficiently modulate immunological dysfunction correlated with LPS-induced AKI: complement inhibition and sCD40L removal are key target to limit sepsis-associated AKI and multiple organ dysfunction. PMMA membrane should be investigated in future clinical trials even based on sequential therapy of CVVH added to devices for LPS removal.

Abstract Category: F) RRT Research

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Nonrenal Outcomes of Pediatric Continuous Kidney Support Therapy (CKST) Patients

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[1]*Texas Children's Hospital, Houston, TX, USA,* [2]*Seattle Children's Hospital, Seattle, WA, USA*

Post-intensive care syndrome in pediatrics (PICS-p) is associated with significant morbidity, disproportionately impacting those with severe multiple organ failure requiring organ support. We previously showed pediatric CKST survivors are at high risk of new morbidity at ICU discharge using Functional Status Scale (FSS). Despite its superior granularity, FSS depends on accurate documentation of six different domains (mental status, sensory, communication, motor function, feeding, and respiratory). Less granular qualitative functional metrics, Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance Category (PCPC) might be useful where access to accurate documentation is limited to accurately capture functional status to identify patients at high risk of PICS-p.

Methods: We compared global functional status in pediatric CKST patients using FSS, POPC and PCPC at hospital discharge. We performed a case-control study with age and severity of illness matched controls with similar functional status at baseline to compare functional outcomes.

Results: We included 89 (58% male) CKST patients and 45 (60% male) controls. Median CKST duration was 12 days (IQR 5-23). 91% of the CKST and 82% of controls were mechanically ventilated. Admission Pediatric Logistic Organ Dysfunction (PELOD) was comparable and premorbid baseline FSS was normal in both groups; FSS at hospital discharge was significantly higher(=worse) in CKST (11 (8-30) vs 7 (6-11), $p<0.001$). At hospital discharge, CKST patients had worse functional outcomes adjudicated by PCPC vs controls (good (21 vs 56%), mild disability (15 vs 7%), moderate disability (3 vs 13%), severe disability (21 vs 11%), vegetative state or coma (1 vs 2%) and death (35 vs 11%), CKST vs control, respectively, $p<0.001$). POPC outcome adjudication was also similar. Discharge FSS scores were tightly correlated with both POPC and PCPS ($p<0.001$) in cases and controls, despite having more dispersion in higher POPC and PCPC categories, suggesting less precision with the simplified scores (POPC=4, median FSS 11 (range 6-24); PCPC=4, median FSS 11 (range 7-24)). Baseline FSS and admission PELOD were significant predictors of discharge POPC and PCPC for controls but not for CKST patients.

Conclusion: Simpler classification provided by POPC and PCPC tools could be used to adjudicate functional outcomes in pediatric CKST patients. External validation is needed to assure generalizability in different healthcare settings.

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Comprehensive Multiscale Computational Model of Fluid and Species Transport in Hollow Fiber Membranes

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[1]*LSU Health Shreveport*

Background: In a previous presentation at this conference, we presented a computational model of simple fluid and single-solute transport in a finite element model of a hollow fiber hemofilter. This model has undergone extensive additional development to include the following capabilities: 1) fluid transport in blood, membrane and dialysate phases, 2) influence of plasma oncotic pressure and concentration polarization on ultrafiltration, 3) transport of charged and uncharged protein fractions, 4) transport of all major electrolytes with constraint of electroneutrality including transmembrane protein charge difference, 5) protein binding of calcium, 6) acid-base equilibrium, 7) citrate and calcium kinetics during regional anticoagulation, 8) body compartment volume and electrolytes, 8) heat transport, 9) restricted convection due large molecular weights, and 10) membrane electrical potential due to membrane charge density.

Model Description: The multiscale model consists of an axisymmetric finite element model of an AN-69 hollow fiber consisting of blood, membrane and dialysate phases incorporating the physics described above. Boundary conditions were blood inflow velocity and outflow pressure, dialysate inflow velocity and outflow velocity or pressure, concentrations of all chemical species at blood and dialysate inlets, and temperature of blood and dialysate. This spatially distributed model was coupled to well-mixed volume-varying reactors representing body compartments (blood, interstitial, and intracellular fluid). The blood inlet of the hollow fiber received the output of the body blood compartment, and the blood outlet of the hollow fiber was fed as an inlet to the body blood compartment. Additional inlet conditions included calcium chloride and sodium citrate infusions. Chemical equilibrium reactions were included that represented acid-base balance, calcium binding to citrate, and calcium binding to protein.

Validation: Validation of ultrafiltration rate was performed against data published for the AN-69 membrane, with excellent agreement. Validation for sodium transport was validated against two clinical cases of hypertonic saline dialysis for controlled hypernatremia following brain injury. Validation of other model components is currently being conducted.

Summary: This comprehensive multiscale model can simulate multiple transport processes simultaneously, providing insight into fluid and species handling during hemofiltration and hemodialysis.

Abstract Category: F) RRT Research

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Descriptive Analysis of Extracorporeal Support and Renal Replacement Therapy at a Tertiary Hospital during the SARS-CoV-2 Pandemic

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Background:
Extracorporeal membrane oxygenation (ECMO) is increasingly used in critically ill patients with cardiac and/or respiratory failure. Acute kidney injury (AKI) is common in patients receiving ECMO, often necessitating use of continuous renal replacement therapy (CRRT) to optimize fluid balance and correct electrolyte abnormalities. There are few studies characterizing patients on both ECMO and CRRT. The principal aim of this analysis is to describe demographic and qualitative trends observed in patients receiving both therapies.

Methods:
We performed a retrospective analysis of patients receiving ECMO and CRRT simultaneously at a tertiary care hospital from 2019-2021. All patients requiring CRRT underwent continuous venous-venous hemodiafiltration (CVVHDF). We analyze age, gender, ECMO and CRRT durations of therapy, etiology of CRRT initiation, hospital length of stay (LOS), and mortality to evaluate trends in this cohort. Statistical analyses were performed using JMP 16.0 (Cary, NC) and Excel 2018 (Redmond, WA).

Results:
Our analysis included 99 patients who underwent concomitant ECMO and CRRT support. Mean age was 49.8+/-14.4 years, and 65% were male. The racial and ethnic composition was 57% Caucasian, 39% African American, 1% Hispanic, and 1% Asian. The average hospital LOS was 65.7+/-56.4 days. 18% of patients had known kidney disease prior to admission. The most common causes of AKI necessitating CRRT initiation were septic shock (69%), cardiogenic shock (18%), and post-operative hypotension (4%). Mortality rate for the cohort was 69% (68 patients). Of the 31% of patients who survived, 9 achieved full renal recovery by hospital discharge.

Conclusion:
Our study is one of the largest conducted on patients receiving simultaneous CRRT and ECMO. These patients receiving CRRT and ECMO have a diverse background and high mortality rate; however, survivors may still recover renal function. Further studies identifying factors that influence survival and enhance renal recovery are warranted to improve clinical outcomes in this setting.

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Combined ECMO/CRRT Support in SARS-CoV-2: A Comparative Study

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Background:
Deployment of extracorporeal membrane oxygenation (ECMO) for patients with cardiac and/or respiratory failure has increased in the critical care setting, particularly with the rise in SARS-CoV-2 infections. Acute kidney injury (AKI) is common, often necessitating continuous renal replacement therapy (CRRT) for volume and electrolyte management. Few studies comparing patient outcomes for organ failure from SARS-CoV-2 versus non-SARS-CoV-2 exist. We sought to evaluate differences in outcomes between SARS- and non-SARS-CoV-2 patients that received both ECMO and CRRT.

Methods:
We retrospectively analyzed patients receiving both ECMO and CRRT at a tertiary care hospital between 2019-2021. All patients underwent continuous venous-venous hemodiafiltration (CVVHDF). Patients were subsequently categorized into non-SARS-CoV-2 and SARS-CoV-2 cohorts. Data collected included serum creatinine (SCr) on admission, SCr at the time of CRRT initiation, ECMO parameters, ECMO and CRRT durations, and clinical outcomes. Statistical analyses were performed using JMP 16.0 (Cary, NC) and Excel 2018 (Redmond, WA).

Results:
Our analysis included 99 patients with a mean age of 49.8 +/- 14.4 years. Of the entire cohort, 35% were hospitalized for SARS-CoV-2 infection. A greater proportion of patients in the non-SARS-CoV-2 group had baseline kidney disease prior to admission (28.3% vs 9.1%; p=0.03). Mean SCr on admission for non-SARS-CoV-2 and SARS-CoV-2 cohorts were 1.98+/-2.04 mg/dL and 1.61+/-0.92 mg/dL, respectively (p=0.11). Mean SCr at CRRT start for the non-SARS-CoV-2 and SARS-CoV-2 cohorts was 3.46+/-1.58 mg/dL and 2.87+/-1.17 mg/dL, respectively (p=0.025). At the time of discharge or death, mean SCr in the non-SARS- and SARS-CoV-2 groups was 1.78+/-1.56 mg/dL and 1.35+/-0.84, respectively (p=0.041). Patients without SARS-CoV-2 were on CRRT for an average of 24+/-20.7 days, while patients with SARS-CoV-2 were on CRRT for 40+/-31.5 days (p=0.99). Mean ECMO duration for non-SARS-CoV-2 vs. SARS-CoV-2 was 28.3+/-29 days and 45.4+/-43 days, respectively (p=0.98). The mortality rates of patients receiving both CRRT and ECMO for SARS-CoV-2 vs non-SARS-CoV-2 cohorts were 73.5% vs 63.2% (p=0.45), respectively.

Conclusion:
Our findings suggest that patients with SARS-CoV-2 infection had lower serum creatinine at the

initiation and conclusion of CRRT. There were no significant differences in CRRT or ECMO duration. Both cohorts had similar, albeit high, mortality rates. Additional patient enrollment and research are needed to better support these trends with a greater degree of confidence. Utilization of novel markers of renal function would also provide further insight into the relationship between SARS-CoV-2 and acute kidney injury severity.

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Pediatric Continuous Renal Replacement Therapy Float Nurse Role

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Purpose: Continuous Renal Replacement Therapy (CRRT) is a low-use, high-risk therapy in many pediatric hospitals. We designed and implemented a clinical nursing model that supports pediatric critical care nurses providing care to patients receiving CRRT. Similar to the Charge Nurse or the Rapid Response Team Nurse assignment each shift, the Pediatric CRRT Float Nurse is a designated role activated when CRRT is prescribed in one of the pediatric ICUs, designed to support patient safety. This role must be filled by a CRRT superuser, defined as a pediatric intensive care nurse with advanced training in CRRT filter starts. Staffing expenses are transferred to correlate with the revenue stream.

Background: There are limited CRRT devices available for use to deliver pediatric CRRT. Mott Children's Hospital, like our colleagues nationally, adapt current CRRT technology to safely care for patients weighing less than 20 kilograms. Greatest adaptation is needed for patients weighing less than 8 kilograms. The CRRT Float Nurse Role was created in response to patient safety events surrounding filter starts or care of the pediatric CRRT patient, focusing on preparing for filter start, calculating fluid removal, alarm troubleshooting, and regional anticoagulation delivery and monitoring.

Summary: Nurse leaders from this institution identify the CRRT Float Nurse as a valuable support to the bedside nurse caring for the pediatric CRRT patient. The CRRT Float Nurse is able to prepare for filter starts in consultation with the pediatric nephrologist, perform filter starts without interruption, provide just in time support for the bedside CRRT nurse, respond to unexpected CRRT circuit work, and provide early intervention.

Conclusion: The CRRT Float Nurse role is vital component of this institution's CRRT nursing model, providing structured support for nurses caring for pediatric CRRT patients, contributing to safe delivery of CRRT.

CRRT Float Nurse Expectations:
Set up CRRT devices including blood, 5% albumin, and saline primed filters
Review orders, CRRT fluid calculation, and documentation
Complete CRRT circuit assessments and safety checks
Round with pediatric nephrology on CRRT patients to ensure aligned goals of care
Review high risk alarm troubleshooting with bedside nurse
Support the bedside nurse in CRRT interventions i.e., discontinuing CRRT, trial off of VA ECMO
Provide rapid dissemination of practice changes

Abstract Category: G) Nursing Issues

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Cultivating a CRRT Education Program to Meet the Demand of an Everchanging Workforce

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Over the past several years, there has been a noticeable increase in the need for Continuous Renal Replacement Therapy (CRRT). Critical care patients are presenting with a higher acuity than we have ever seen before. Factors such as complex Acute Kidney Injury (AKI), multiple comorbidities, and complications of COVID-19 have contributed to the increase in patient acuity and the growing need for CRRT. The nurses caring for these critical patients need to be highly skilled and experienced. Due to burnout and nursing turnover, there is a large gap in the number of experienced nurses trained to perform CRRT. Training a multi-experienced workforce to perform CRRT requires a concise, standardized education program to equip the ICU Registered Nurse (RN) with the necessary skills to provide safe, quality care.

Below is the training program created to meet the growing need for highly skilled and competent CRRT nurses.
I. Program Design
a. Pre-requisite web-based training modules
b. Interactive case scenario led presentation
c. Hands on experience with machine management
d. Hemodialysis catheter access and de-access
II. Real time education opportunities
a. Daily rounding on all CRRT patients
b. RN support with set up, maintenance, and troubleshooting
c. Discussion of CRRT utilization during multidisciplinary rounds
III. Education program modifications during the pandemic
a. Converted to a virtual platform
b. Temporary workforce added to CRRT training
c. Identified wins and opportunities
IV. Advanced User Training
a. Standardization of CRRT practices
b. Offers experienced CRRT RNs additional education
V. Future State
a. Develop a hybrid classroom model
b. Revamp hands on CRRT skills checkoff
c. Establish an annual competency validation

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Reality, Simulation The Same

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Introduction
The pediatric incidence of patients diagnosed with acute kidney injury requiring continuous renal replacement therapy (CRRT) is rising. Increased use of extracorporeal therapies paired with the ever-changing healthcare workforce requires high-quality training for a successful program. A more robust educational experience was identified as a need within a CRRT specialty team to increase confidence and consistency with setup, management, and problem-solving the CRRT circuit. Collaboration with the simulation department showed potential in providing a more realistic and interactive experience than existed. A novel CRRT simulation program was developed to mimic real-time complications with both the CRRT pump, and the patient requiring clinicians to think and react in a high-stress environment.

Methods
Educational needs were gathered by reported events, feedback from team members, and a needs assessment. The previous educational method of water drills did not produce the high-level experiential learning sought after by the CRRT Coordinator. We first researched ways to enhance the level of training by contacting other CRRT centers around the region. Although unsuccessful in finding an existing program that met their needs, it was decided to shadow an established simulation program and design a new program. The coordinator, a team champion worked with the simulation department to create a system replicating realistic pump pressures and clinical situations that required high-level critical thinking and troubleshooting. Trial runs and countless hours of concept design led to the first successful CRRT Simulation course.

Results
Twenty-one team members completed the first round of CRRT simulation. The sessions were 4-hour blocks, included four scenarios, with a facilitated debriefing following each scenario in the simulation lab. Debriefing allowed for discussion of educational topics, identification and remediation of process gaps, and opportunities for standardizing care within the team. Feedback from the nursing staff was unanimously positive and worth the time.

Discussion/Conclusion
To truly probe the system and enhance the quality of training, CRRT nurses need the ability to interact with a CRRT pump and patient as close to real-life as possible. Designing a CRRT Simulation program has proven beneficial to increase the knowledge and comfort level of the nurses while standardizing education and care of the patient and pump.