Abstracts

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Updates in ICU Medicine: Controversies, Challenges and Solutions

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EPIDEMIOLOGY AND OUTCOMES FROM AKI

Abstract/Poster Number

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RESEARCH II

EPIDEMIOLOGY AND OUTCOMES FROM AKI

1

Albumin is a Prognostic Factor in Patients with Acute Kidney Injury receiving Continuous Renal Replacement Therapy therapy in critically ill patients with acute kidney injury

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Background: This study aimed to assess how hypoalbuminemia (albumin <3.0 g/dL) affects the outcomes of patients treated with Continuous Renal Replacement Therapy
Methods: We collected data from 1,549 patients with acute kidney injury who received continuous renal replacement therapy from October 2012 to August 2018. Patients without albumin values on the first day of Continuous Renal Replacement Therapy (n=159) were excluded. Data from 1,390 patients were analyzed. Patients were divided into two groups: those with albumin levels < 3.0 g/dL (n=684) and those with albumin levels ≥ 3.0 g/dL (n = 706).
Results: Patients with albumin levels < 3.0 g/dL had a mortality rate of 59.8%; the mean albumin value on the first day of continuous renal replacement therapy was 2.49 g/dL. Patients with albumin levels ≥ 3.0 g/dL had a mortality rate of 38.1% with a mean value of 3.53 g/dL on the first day of continuous renal replacement therapy. Patients were lower albumin levels (<3.0 g/dL) had significantly higher mortality rates($p < 0.001$; Table 1). Table 2 shows the treatment characteristics pertaining to continuous renal replacement therapy for the two groups. There were no statistical differences in the clinical settings between the two groups. We found that hypoalbuminemia (<3.0 g/dL) was a prognostic factor in patients with acute kidney injury requiring continuous renal replacement therapy. We also found that the Acute Physiology, Age, Chronic Health II score was a prognostic factor ($p < 0.001$).
Conclusion: The results show that hypoalbuminemia (<3.0 g/dL) is a significant predictor of mortality in patients with acute kidney injury receiving continuous renal replacement therapy.

2

Changing Epidemiology and Outcomes of AKI Patients in Teachng Hospital from a Developing Country: a Population-based Cohort Study

Welder Zamoner[1], Vanessa Addad[1], Andre Balbi[1], Marci Batistoco[1], Daniela Ponce[1]

[1]*University of Sao Paulo State - Botucatu School of Medicine*

Background: Epidemiology and outcome for AKI vary according to geographic region and socioeconomic status. While considerable information is available on AKI in North America and Europe, large comprehensive epidemiologic studies of AKI from Latin America are still lacking. The present study is the largest cohort providing AKI patient characteristics and their relationship to outcomes in a Brazilian center. The aim was to evaluate the epidemiology and outcome of AKI in patients evaluated by nephrologists in a teaching Brazilian hospital across time periods. Methods: We performed a retrospective observational study of AKI patients evaluated by nephrologists in a Brazilian teaching hospital from Jan 2011 to Dec 2018. Study was undertaken to

look into epidemiology for AKI and its effect on patient outcome across period time. AKI status was defined according to KDIGO 2012 criteria. For comparison purposes, patients were divided into two groups according to the year of follow up: 2011-2014 and 2015-2018. Multivariable logistic regression was used to adjust confounding and patient survival was analyzed using the competing risk model of Fine and Gray. Significance p level was 0.05. Results: We enrolled 7,976 Brazilian AKI patients evaluated by nephrologists from Jan 2011 to Dec 2018. After excluding patients with Chronic Kidney Disease stages 3 to 5, kidney transplanted and those with incomplete data, 5,428 AKI patients were included (68%). Overall, the maximum AKI stage was Stage 3 in 50.6%, Stage 2 in 33.1%, Stage 1 in 13.1%, acute on chronic 3.2% and mortality rate occurred in 1865 patients (34.3%). Dialysis treatment was indicated in 928 patients (17.1%). Patient survival improved along study periods: compared to 2011-2014 patients treated at 2015-2018 had a relative risk death reduction of 0.89 (95% CI 0.81 – 0.98, p=0.02). The independent risk factors for mortality were sepsis, older > 65 anos, admission to ICU, AKI-KDIGO 3, Acute Tubular Necrosis index specific score (ATN-ISS) >0.65, recurrent AKI, no metabolic and fluid demand to capacity imbalance as dialysis indication and the period of treatment. Conclusions: We observed an improvement in AKI patient survival evaluated by nephrology team along the years. This finding was sustained even after correction for several confounders and using a competing risk approach. Identification of risk factors for mortality can help in decision making for timely intervention, leading to better clinical outcomes.

3

Serum concentration of vancomycin is a diagnostic predictor of nephrotoxic acute kidney injury in critically ill patients

Welder Zamoner[1], Karina Zanchetta[1], Andre Balbi[1], Adriano Santos[1], Daniela Ponce[1]

[1]*University of Sao Paulo State - Botucatu School of Medicine*

There are few studies evaluating the monitoring of plasmatic concentration of vancomycin in septic patients and their association with acute kidney injury (AKI) and death. This study aims to evaluate the prevalence of subtherapeutic and toxic serum concentrations of vancomycin in hospitalized septic patients and to associate the adequation of therapeutic monitoring with clinical outcomes. Methodology: Cohort unicentric study who evaluated patients older than 18 years using vancomycin admitted to intensive care units (ICU) of a Brazilian University Center in the period from August 2016 to July 2017 in a daily and uninterrupted way. Were excluded patients with AKI prior to the introduction of vancomycin or with AKI development in less than 48 hours after their use, patients with AKI of other etiologies, stage V of chronic kidney disease and pregnant women. Results: 182 patients were evaluated and 63 patients were included. The measurement of serum concentration of vancomycin was performed in 92% of the patients and 58.7% were at a toxic level. The prevalence of AKI was 44.4% and occurred on average on the 6th day of use of vancomycin. Between 2nd and 4th day, vancomycin above 17.53 mg/L was shown to be a predictor of AKI with an area under the curve of 0.806 (IC 95% 0.624-0.987, p=0.011) preceding the diagnosis of AKI for at least 2 days. Of these patients, 46.03% died and in the analysis of Cox, the age was the single factor associated with the death. Conclusion: Serum concentration of vancomycin is an excellent predictor of AKI in critical patients, preceding the diagnosis of AKI in at least 48hours. Although guidelines recommend therapeutic concentrations between 15 and 20mg/L for patients at ICU, the results of this study suggest that the target of monitoring should be between 15 and 17.5mg/L.

4

The role of vancokinemia in the non-critical population as a diagnostic and prognostic predictor of acute kidney injury.

Welder Zamoner[1], Karina Zanchetta[1], Andre Balbi[1], Adriano Santos[1], Daniela Ponce[1]

[1]*University of Sao Paulo State - Botucatu School of Medicine*

Vancomycin is a strategic antimicrobial in the treatment of serious Gram positive germ infections, which although it has used for over 60 years, there are still questions about its efficacy and safety. There are few studies evaluating the monitoring of its plasma level in non-septic patients and its association with clinical outcomes, such as the development of acute kidney injury (AKI) and death. Objective: This study aimed to evaluate the role of vancokinemia in the non-critical population as a diagnostic and prognostic predictor of AKI vancomycin-associated. Methods: We performed a unicentric cohort study that evaluated patients older than 18 years using vancomycin and admitted to clinical and surgical wards of a Brazilian teaching hospital from August 1, 2017 to July 31, 2018, daily and uninterrupted. Patients with AKI prior to the introduction of vancomycin or who developed AKI less than 48 hours after use, patients with AKI of other etiologies, chronic kidney disease patients stage 4 and 5 and pregnant women were excluded. Two clinical outcomes were evaluated: AKI development and death. Results: A total of 225 patients were evaluated, including 135 non-critically ill patients. Serum vancomycin levels were measured in 94.1% and 59.3% of these were toxic concentrations (> 20 mg/L). The prevalence of AKI was 27.4% and occurred on average on the 9th day of vancomycin use. Between the 4th and 6th day, a vancokinemia value above 21.5 mg/L was predictor of AKI with an area under curve (AUC) of 0.803 (95% CI 0.625-0.98, p = 0.005) preceding the diagnosis of AKI in at least 3 days. Logistic regression identified as factors associated with AKI the use of vasoactive drugs, and vancomycin toxic concentrations. Of these patients, 20.7% died. AKI and older age were identified as risk factors for death. Conclusion: Vancokinemia is an excellent predictor of AKI in patients admitted to wards, preceding AKI diagnosis in at least 48 hours. Toxic vancokinemia concentrations are associated with AKI, while AKI is risk factor for death.

5

Comparison of Outcomes According to Urine Chemistry Testing Time for the Causes of Acute Kidney Injury Patients Admitted to the Emergency Room

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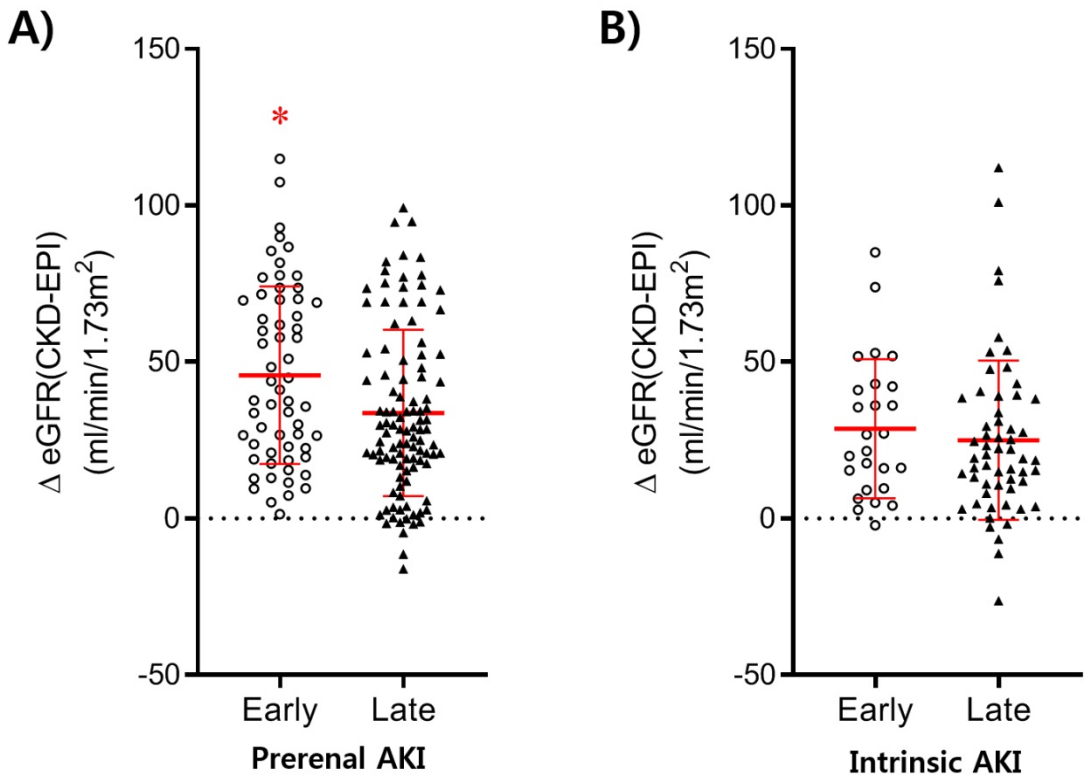
Introduction: Rapid identification and treatment of acute kidney injury can help to restore kidney function. In order to differentiate between prerenal AKI and intrinsic AKI, we perform a urine chemistry test to determine the function of the renal tubule. However, there is no report that it is helpful to arrive at the hospital as early as possible and to perform these urine chemistry tests as soon as possible.

Methodology: We analyzed the timing of urinary chemistry in AKI patients who were admitted to our hospital through the emergency room for 3 years and divided into two groups. Early group was defined as patients who

performed the test within 3 h of arrival in the emergency room. Late group was defined as patients who were late or not. The prognostic factors were change in 30 day eGFR and duration of hospital stay. We also compared the usefulness of urine chemistry test between prerenal AKI and intrinsic AKI in each group.

Results: The changes of eGFR after 30 days in each group are 41.6 ± 27.6 mL/min/1.73 m2 (Early group, n = 92) vs 30.4 ± 26.8 mL/min/1.73 m2 (Late group, n = 180) (P = 0.0013). Early group patients were discharged more quickly than patients in the late group (Hospital day: 11.5 ± 10.1 vs 13.8 ± 10.5, P = 0.0450). When analyzed according to the causes of AKI, these changes showed differences in prerenal AKI rather than intrinsic AKI.

Conclusions: A urine chemistry test is a test to help determine the cause of AKI. Based on the results of urine chemistry performed within 3 h after arrival at the hospital, patients with AKI who visited the emergency room had better improved kidney function and less hospitalization.



6

Metabolic acidosis as a risk factor for the development of acute kidney injury and hospital mortality

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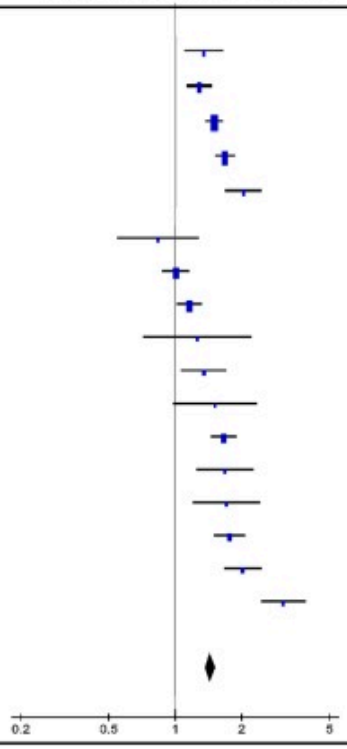
Metabolic acidosis has been proved to be a risk factor for the progression of chronic kidney disease, but its relation to acute kidney injury (AKI) has not been investigated. In general, a diagnosis of metabolic acidosis is based on arterial blood gas (ABG) analysis, but the diagnostic role of carbon dioxide combining power (CO2CP) in the venous blood may also be valuable to non-respiratory patients. This retrospective study included all adult non-respiratory patients admitted consecutively to our hospital between October 01, 2014 and September 30, 2015. A total of 71,089 non-respiratory patients were included, and only 4,873 patients were evaluated by ABG analysis at admission. In patients with ABG, acidosis, metabolic acidosis, decreased HCO3- and hypocapnia at admission was associated with the development of AKI, while acidosis and hypocapnia were independent predictors of hospital mortality. Among non-respiratory patients, decreased CO2CP at admission was an independent risk factor for AKI and hospital mortality. ROC curves indicated that CO2CP was a reasonable biomarker to exclude metabolic acidosis, dual and triple acid-base disturbances. The effect sizes of decreased CO2CP on AKI and hospital mortality varied according to age and different underlying diseases. Metabolic acidosis is an independent risk factor for the development of AKI and hospital mortality. In non-respiratory patient, decreased CO2CP is also an independent contributor to AKI and mortality and can be used as an indicator of metabolic acidosis.

	Decreased CO2CP		Normal CO2CP			
Incidence of AKI	AKI	Total	AKI	Total	OR (95%CI)	Favors normal Favors decreased
Age						
18-34	166	1746	276	3800	1.34 [1.10, 1.64]	
35-49	324	3460	768	10279	1.28 [1.12, 1.47]	
50-64	717	6001	1946	23412	1.50 [1.37, 1.64]	
65-79	563	3732	1438	14978	1.67 [1.51, 1.86]	
≥80	207	949	330	2732	2.03 [1.68, 2.46]	
Underlying diseases						
Gynecological	33	667	71	1216	0.84 [0.55, 1.28]	
Cardiothoracic surgery	429	1048	1323	3253	1.01 [0.88, 1.16]	
Cancer	357	2054	1014	6614	1.16 [1.02, 1.33]	
Endocrine	18	621	40	1734	1.26 [0.72, 2.22]	
Hematological	126	768	226	1783	1.35 [1.07, 1.71]	
Renal	29	385	85	1670	1.52 [0.98, 2.35]	
General surgery	343	2398	730	7998	1.66 [1.45, 1.91]	
Neurological	79	571	128	1471	1.68 [1.25, 2.27]	
Orthopedic surgery	49	847	98	2833	1.71 [1.21, 2.44]	
Cardiovascular	226	3513	515	13771	1.77 [1.51, 2.08]	
Others	164	1587	326	6066	2.03 [1.67, 2.47]	
Digestive	124	1429	202	6792	3.10 [2.46, 3.91]	
Total	1977	15888	4758	55201	1.45 [1.37, 1.54]	



7

Volume Associated Hemodynamic Variables for Prediction of Severe Acute Kidney Injury and Renal Replacement Therapy after Cardiac Surgery

Jiarui Xu[1], Wuhua Jiang[1], Bo Shen[1], Ziyan Shen[1], Yimei Wang[1], Zhe Luo[2], Chunsheng Wang[3], Jie Teng[1], Xiaoqiang Ding[1], Jiawei Yu[1]

[1]*Nephrolong, Zhongshan Hospital,* [2]*Critical Care Medicine, Zhongshan Hospital,* [3]*Cardiovascular Surgery, Zhongshan Hospital*

Background: Delayed diagnosis of acute kidney injury (AKI) is common because changes of renal function markers often lag injury. We aimed to find optimal volume associated hemodynamic variables for the prediction of postoperative AKI, severe AKI and renal replacement therapy (RRT).
Methods: Data were collected from 1,180 patients who underwent cardiac surgery in our hospital between March 2015 and Feb 2016. Postoperative central venous pressure (CVP), mean arterial pressure (MAP), heart rate (HR), PaO2 on ICU admission, dose of vasoactive agent and percentage of fluid overload (PFO) were monitored and compared between AKI vs. non-AKI, severe AKI vs. non-severe AKI and RRT vs non-RRT cases.
Results: The AKI, severe AKI and AKI-RRT incidences were 36.7% (n=433), 9.7% (n=115) and 1.2% (n=14). CVP on ICU admission was significantly higher in AKI, severe AKI and RRT groups (11.5±3.1 vs 9.0±3.0 mmHg, P<0.001; 12.7±2.7 vs. 9.6±2.9 mmHg, P<0.001; 13.3±2.5 vs 9.9±3.0 mmHg, P< 0.001). Low cardiac output syndromes (LCOS) occurred significantly more in AKI, severe AKI and RRT groups than in non-AKI, non-severe AKI and non-RRT groups (13.2 vs 3.9%, P<0.001; 24.3% vs. 5.7&, P<0.001; 42.9% vs 7.1%, P<0.001). Proportion of 24h PFO>5% in AKI, severe AKI and AKI-RRT group were significantly higher (9.2% vs. 2.4%, P<0.001; 15.7% vs. 3.8%, P<0.001; 35.7% vs. 4.5%, P<0.001). Multivariate logistic regression analysis showed that CVP on ICU admission, LCOS and 24 h PFO>5% were always the independent risk factors of AKI, severe AKI and AKI-RRT. The area under the ROC curve to predict postoperative AKI by combining CVP on admission (>11mmHg) + LCOS + 24PFO (>5%) was 0.763. The area under the ROC curve to predict severe AKI by CVP on ICU admission (>12mmHg) + LCOS + 24PFO (>5%) was 0.758. The area under a ROC curve to predict AKI-RRT by CVP on admission (>13 mmHg)+LCOS+24 h PFO (>5%) was 0.886.
Conclusion: The volume associated hemodynamic variables including CVP on ICU admission, LCOS and 24 h PFO could predict postoperative AKI, severe AKI and AKI-RRT accurately.

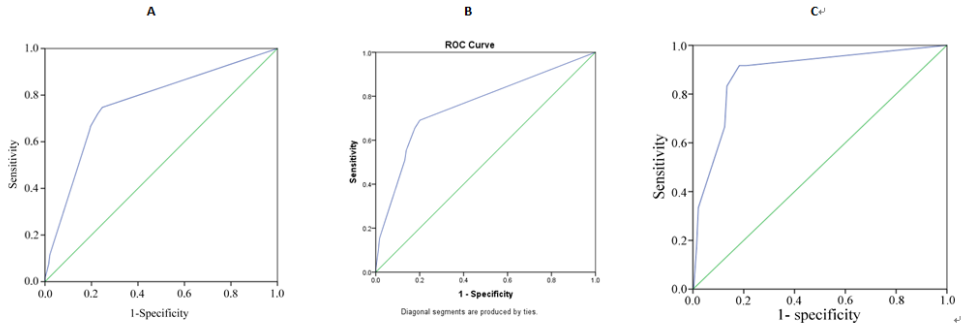


Figure (A) The area under the ROC curve to predict postoperative AKI by CVP on ICU admission (>11mmHg) + LCOS + 24h PFO (>5%) was 0.763.

(B) The area under the ROC curve to predict severe AKI by CVP on ICU admission (> 12 mmHg) + LCOS + 24 h PFO (> 5%) was 0.758.

(C) The area under the ROC curve to predict AKI-RRT by CVP on ICU admission (> 13 mmHg) + LCOS + 24 h PFO (> 5%) was 0.886.

8

Incidence and long term prognosis of different cardiac surgery associated acute kidney injury

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Background:
Dialysis requiring Acute kidney injury (D-AKI) is a major complication of cardiovascular surgery, which results in worse short-term and long-term prognosis. However, the impact of D-AKI on outcomes among different cardiac surgeries has not been fully investigated.
Methods:
We identified patients who were admitted for cardiovascular surgery between July 1, 2004 and December 31, 2013 from Taiwan National Health Insurance Research Database. Patients were grouped into the dialysis needed AKI (n=3089) group and the non-AKI (n=42151) group. Inverse probability of treatment weighting (IPTW) was performed to mitigate confounding. The primary outcome was all-cause of mortality and secondary outcome was major adverse kidney event (MAKE).
Result:
D-AKI has higher risks of hospital mortality (odds ratio [OR]: 27.96, 95% CI: 26.32–29.69), stroke, respiratory failure, and had more medical expenditure (D-AKI: 29.2 USD×103 and non-D-AKI: 14.7 USD×103). Late outcomes were worse in the D-AKI group than the non-D-AKI group (hazard ratio [HR]: 3.89 and 95% CI: 3.79–3.99 for MAKE; HR: 2.89 and 95% CI: 2.81–2.98 for all-cause mortality). Patients who received aorta surgery had higher risk for D-AKI than other surgery types but were more likely to recover. Among patients with valve heart surgery, the observed increased risks of all-cause mortality (OR:6.04, 95% CI: 5.78－6.32) and MAKE (OR:6.49, 95% CI: 6.26－6.76) was the greatest when compared to other surgeries.
Conclusion:
The incidence of D-AKI and its outcome after cardiac surgery varied from the surgical type and reflected its underlying disease. In comparison to heart surgery, aortic surgery resulted in higher incidence of dialysis-AKI but less incidence of long-term dialysis and MAKE. D-AKI in after valve surgery worsens survival and MAKE than other surgical types.

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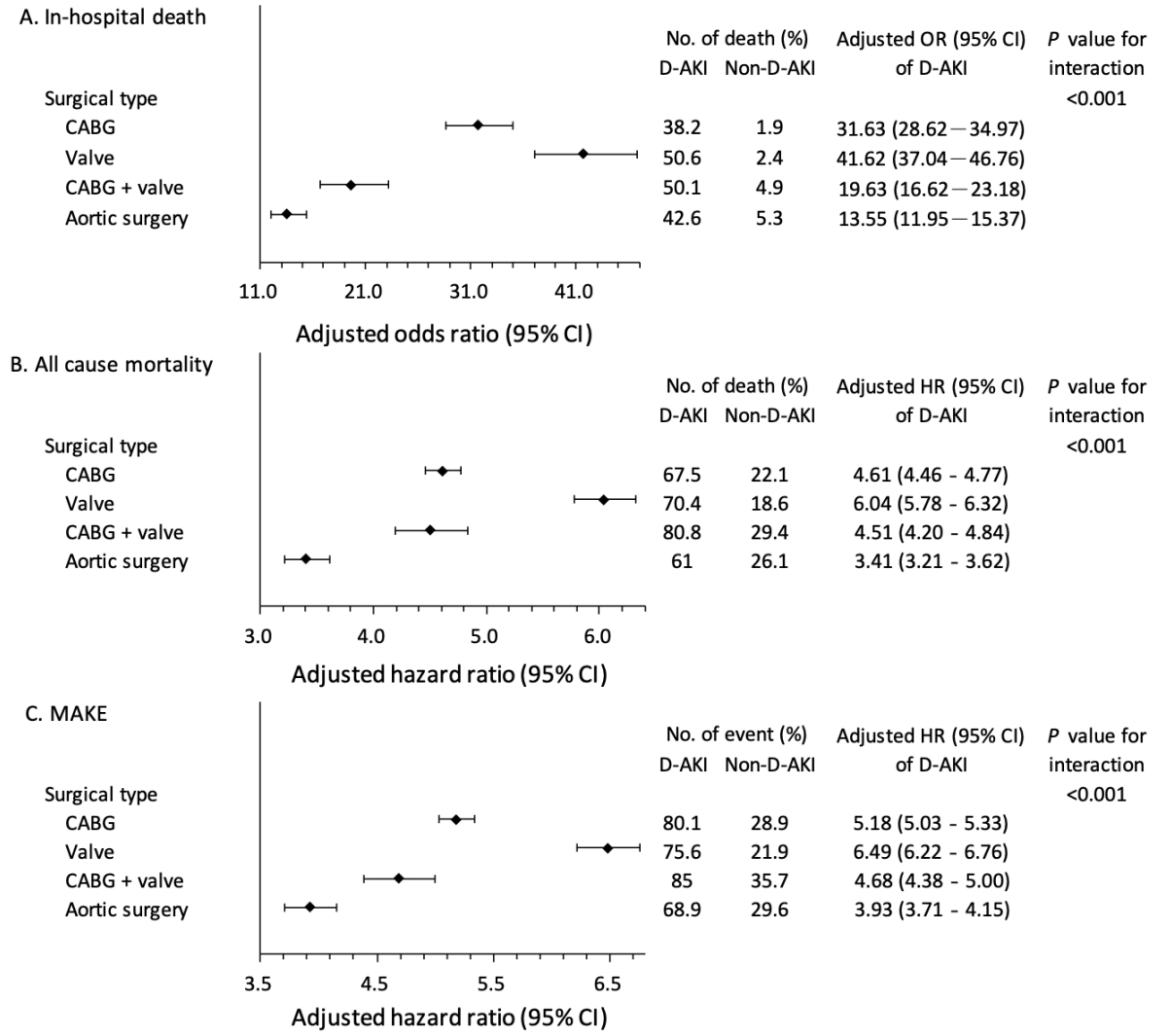


9

Renal-cardio Multidisciplinary Team Decreased the Incidence and Mortality of Severe Acute Kidney Injury after Cardiac Surgery: Experience from 8-year cohort

Jiawei Yu[1], Jiarui Xu[1], Yimei Wang[1], Jie Teng[1], Jiachang Hu[1], Wuhua Jiang[1], Bo Shen[1], Zhe Luo[2], Chunsheng Wang[3], Xiaoqiang Ding[1]

[1]*Nephrology, Zhongshan Hospital,* [2]*Critical Care Medicine, Zhongshan Hospital,* [3]*Cardiovascular Surgery, Zhongshan Hospital*

Objective: Acute kidney injury (AKI) is a common and severe complication of cardiac surgery. In recent years, effective approaches to the prevention and management of cardiac surgery associated AKI have developed. Methods: The study was spanned form January 2009 to December 2016. We set up the renal-cardio multidisciplinary team (MDT) since 2014 and a series of practices for AKI managements were adopted. The MDT managements were mostly from KDIGO guideline and our experience. An interrupted time series (ITS) analysis were performed to evaluate the effects of MDT strategies on AKI incidence and in-hospital mortality between pre-MDT period (2009-2013) and post-MDT period (2014-2016).

Results: A total of 21,018 cardiac surgeries were enrolled. The overall AKI incidence was 33.9% (n = 7,134). The incidence of severe AKI (AKI stage 2-3) and AKI-RRT was 8.7% (n = 1,836) and 2.0% (n = 419), respectively. There was no statistical significance of AKI incidence between post-MDT period and pre-MDT period (36.0% vs 34.9%, P = 0.225). The severe AKI incidence was significantly lower in the post-MDT period (8.7% vs 10.0%, P =0.007). The in-hospital mortality of AKI, severe AKI and RRT patients in post-MDT period were significantly lower than in pre-MDT period (4.5% vs. 7.4%,P<0.001; 13.9% vs. 20.9%, P=0.003; 40.7% vs. 58.9%, P=0.005). The ITS analysis showed a significant decrease in trend of severe AKI incidence (β= 16.247, P=0.038) and in-hospital mortality of severe AKI and AKI-RRT (β= 20.290, P=0.026; β= 50.063, P=0.024) in post-MDT period.
Conclusions: The renal-cardio MDT strategy including preoperative modifiable factors management, precise fluid overload control and hemodynamic directed RRT treatment reversed the increasing trend of incidence of AKI and significantly decreased the in-hospital mortality of severe AKI and AKI-RRT.

Figure 1. Incidence of AKI, severe AKI and AKI-RRT before and after MDT

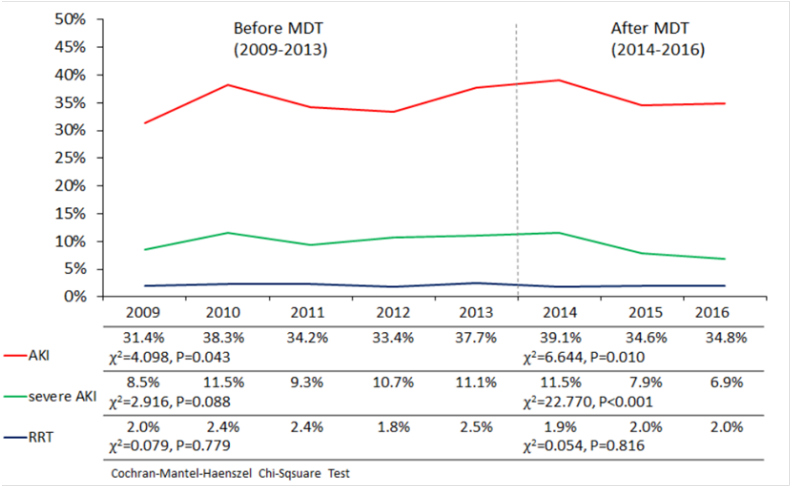
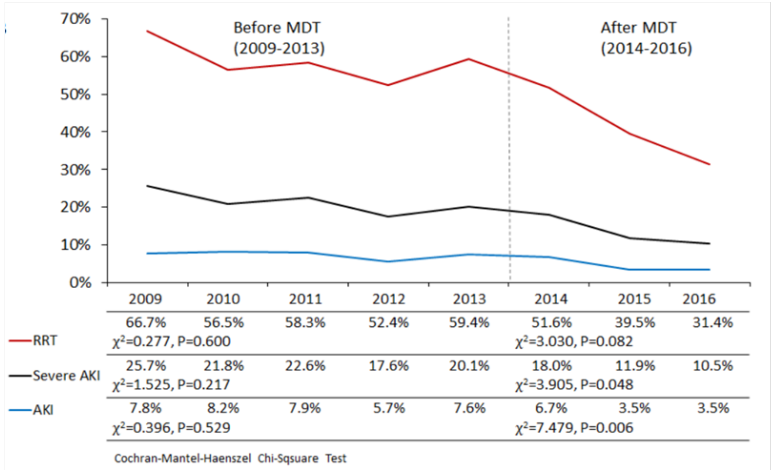


Figure 2. Mortality of AKI, severe AKI and AKI-RRT before and after MDT



10

ACUTE KIDNEY INJURY IN RENAL TRAUMA PATIENTS

Jonathan S Chavez-Iniguez[1], Miguel Ibarra-Estrada[1], Cinthya Cervantes-Sanchez[1], Veronica Valdivia-Cerda[1], Enrique Velarde-Martinez [1], Marisol Lopez-Ceja[1], Rodolfo Moreno[1], Cristian Perez-Flores[1], Pablo Maggiani-Aguilera[1], Guillermo Garcia-Garcia[1]

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Abstract
Kidney is the most commonly injured organ of the genitourinary system during trauma, but little is known about the relationship that this event has with the incidence of acute kidney injury (AKI). In this cohort we describe the associated risk factors for the development of
AKI in patients with renal trauma (RT).

Methods
In a prospective cohort, we analyzed patients with RT during 2015 to 2019 at the Hospital Civil de Guadalajara. We describe their demographic, clinical characteristics and risk factors for development of AKI with univariate and multivariate analysis.

Results.
During the study period 65 patients were analyzed, sixty (92.3%) were men, mechanism
of trauma was firearm in 26 (40%), transfusion was indicated in 18 (25%), and 46 (70%) required emergent surgery, nephrology was consulted in 12 (18%) cases. AKI was present in 39 (60%) patients, only 1 required dialysis. Creatinine and urea at hospital admission was
highest in AKI group (1.56 ± 0.91mg/dL vs. 0.85 ± 0.24mg/dL, p = <0.001 and 56 ± 41mmol/L vs 34 ± 20mmol/L, p = 0.005; respectively). Nephrectomy was not different between those
with 14 (35.9%) and without AKI 5 (19.2), (p=0.15), left kidney is the most affected (57%), Intestine and liver were the most common organs affected (37 and 32%, respectively), there were only 4 deads, all in the AKI group. RT was considered high-grade (4-5) in 37 (56.9%), which has a significant association (p = 0.04) with the incidence of AKI in the univariate analysis, but this association was lost in the multivariate analysis (p = 0.05). We built a model for prediction of AKI with the most relevant variables: firearm injury, shock, emergent surgery, high grade RT, and liver injury (p= 0.02, AUC 0.74).

Conclusion,
RT occurs mainly in young men, 60% of cases are complicated with AKI, the most significant risk factor is high grade RT. It is necessary to confirm this association in other populations and larger sample sizes, which could lead to an earlier and proactive management of AKI.

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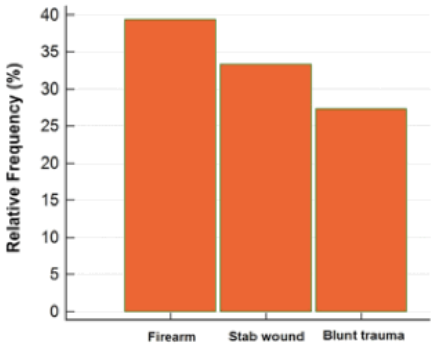

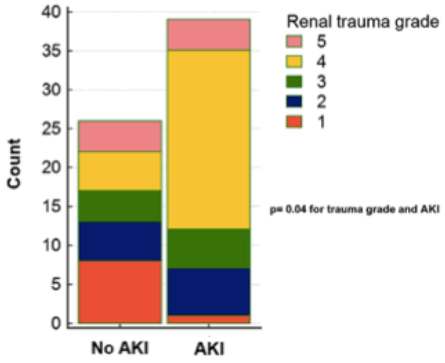

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Relationship between the presence of infectious disease and clinical outcomes of patients with cardiorenal syndrome type 1.

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Introduction:
Cardiorenal Syndrome type 1 (CRS-1) can be triggered by an infection. The pathophysiological basis is vascular congestion, which is why it has been treated with different strategies of diuretics, but in the presence of infection, the inflammatory, neurohormonal and hemodynamic effects can compromise the efficacy of the diuretic therapy and potentially worsen clinical evolution. Here we compare the clinical evolution during the hospitalization of CRS-1 patients with and without infection.
Methods
This is a retrospective cohort study conducted in the Hospital Civil of Guadalajara "Fray Antonio Alcalde", from January 2015 to September 2018. Conducted in CRS-1 patients, we showed the clinical evolution and diuretic strategies analyzed according to the presence or absence of infection. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Results
We identified 63 patients classified as having CRS-1, 28 (44.4%) were classified as having an infectious disease. The mean age was 62 years (±14.6) and 58 (±12.4) in the group with infection and no infection, respectively. There were no statistically significant differences between the clinical outcomes of both groups.

The median length of hospital stay was 8 days in the group with infection and 7 days in the group without infection (p=0.065). Three patients (10.7%) of the group with infection received renal replacement therapy and 1 patient (2.9%) in the group without infection (p=0.315). In the group with infection, 2 patients died (7.1%), whereas in the uninfected group there were no deaths (p=0.194). sCr values tend to diminish in a similar manner in both groups. Serum sodium tend to increase during the hospitalization but there was no significant difference between the groups. We found that all patients received furosemide at least during the first five days of hospitalization and the strategy of the diuretic chosen was similar between groups.

Conclusion

We showed that the clinical evolution of patients with CRS-1 is similar in the presence or absence of infection. We anticipate that this study may be a reason to expand knowledge in patients with CRS-1 and the presence of infection.

Table 2. Evaluation of cardiovascular and renal function

Variables	Cardiorenal syndrome type 1 (N=63)		
	Infection (N=28)	No infection (N=35)	p value
Renal biomarkers			
Creatinine on admission (mg/dL), median (min – max)	2.13 (1.16 - 4.41)	2.28 (1.22 - 5.39)	0.863 μ
Intermediate creatinine (mg/dL), median (min – max)	1.63 (0.76 - 5.73)	1.56 (0.96 - 4.78)	0.961 μ
Creatinine at discharge (mg/dL), median (min – max)	0.98 (0.52 - 6.18)	0.99 (0.44 - 4.94)	0.819 μ
Serum electrolytes			
Sodium on admission (mEq/L), median (min – max)	133 (119 - 146)	136 (116 - 142)	0.215 μ
Sodium at discharge (mEq/L), median (min – max)	136 (129 - 146)	139 (133 - 145)	0.224 μ
Cardiac biomarkers			
NT-pBNP, n (%)	5 (17.8)	9 (25.7)	0.490 £2
NT-pBNP (pg/mL), median (min – max)	6402 (4695 -18020)	2105 (940 - 14837)	0.183 μ
BNP, n (%)	23 (82.1)	26 (74.3)	0.456 £1
BNP (pg/mL), median (min – max)	1520 (443 - 5000)	983 (220 - 2710)	0.048 μ
Echocardiogram			
LVEF (%), median (min – max)	45 (16 - 75)	56 (14 - 74)	0.087 μ
Ischemic cardiomyopathy	5 (17.9)	3 (8.6)	0.271 £2
Hypertensive cardiomyopathy	14 (50)	21 (60)	0.427 £1
Dilated cardiomyopathy	2 (7.1)	3 (8.6)	1.000 £2
Cor pulmonale	12 (42.9)	8 (22.9)	0.090 £1
Other €	2 (7.1)	7 (20)	0.277 £2

€: Degenerative sclerose, revascularization, degenerative.
£1: P value obtained through X^2 test.
£2: P value obtained through Fisher's exact test with a binomial distribution.
μ: P value obtained through the U-Mann-Whitney test for independent variables.
BNP: Brain natriuretic peptide; NT-pBNP: N-terminal pro b-type natriuretic peptide; LVEF: Left ventricular ejection fraction.

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Association between Leptospirosis-associated AKI and Long-term Renal Outcomes：A Nationwide Study in Taiwan

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Purpose: Leptospirosis usually results in acute kidney injury (AKI) and even multiple organ failure requiring renal replacement therapy (RRT) but is associated with favorable short-term outcomes if timely treatment is initiated. Animal studies suggest chronic leptospirosis may develop if leptospira persists in the tubular lumen and interstitium as a continuum of AKI, leading to chronic interstitial fibrosis and progressive kidney failure. However, information on long-term risk of adverse outcome such as chronic kidney disease (CKD) or end stage renal disease (ESRD) after human leptospirosis associated AKI is limited.

Method: We performed a nationwide study used claim data obtained from Taiwan National Health Insurance Research Database. Patients who had an admission for leptospirosis from 2006 to 2013 were identified. To clarify the relationship between leptospirosis associated AKI and long-term risk of kidney failure, patients with prior renal dysfunction, organ transplantation, malignancy, or autoimmune disease were excluded. Ultimately, a study population of 2145 patients with leptospirosis were eligible for analysis. Patients were divided into the non-AKI (n=1702, 79.3%), AKI (n=366, 17.1%), and AKI requiring RRT groups (n=77, 3.6%). The incidence of new-onset CKD or ESRD among the study groups was compared using Fine and Gray subdistribution hazards model, which considered mortality as a competing risk.

Results: The mean follow-up time was 4.3 years. Long-term mortality was higher in the AKI-RRT group than in the AKI group and non-AKI group. Similarly, the incidence rate of CKD was highest in the AKI-RRT group (46.8%) followed by the AKI (34.7%) and non-AKI group (7.0%). Only four patients developed ESRD and all of them were AKI-RRT group. Multivariate Cox analysis revealed that the hazard ratios for the development of CKD in patients with leptospirosis were 6.3 and 8.5 for patients with AKI and AKI-RRT compared with those with non-AKI after adjusting for potential risk factors for CKD.

Conclusions: Leptospirosis-associated AKI may play a critical role in the development of CKD. Additional investigations are warranted to explore the possible mechanisms in human beings.

	HR (95% CI), P value			
	AKI without RRT vs. Non-AKI		AKI with RRT vs. Non-AKI	
Outcome/Model	HR (95% CI)	P value	HR (95% CI)	P value
Chronic kidney disease				
Unadjusted	6.9 (5.3 - 8.8)	<0.001	10.6 (7.2 - 15.4)	<0.001
model 1	6.3 (4.9 - 8.2)	<0.001	7.8 (5.3 - 11.5)	<0.001
Model 2	6.3 (4.8 - 8.1)	<0.001	8.5 (5.7 - 12.6)	<0.001

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Objective: Whether surgery time (workday or weekend) affects the occurrence and prognosis of cardiac surgery associated-acute kidney injury (CSA-AKI) remains unclear and may be influenced by various factors. This study aims to compare the incidence and short-term prognosis of CSA-AKI of patients undergoing surgery on workdays and weekends to determine the effect of surgery time.
Methods: The clinical data of patients undergoing cardiac surgery from April 2016 to December 2016 were retrospectively collected. Patients were divided into workday groups and weekend groups based on the surgery completion time. The primary endpoints were the incidences of CSA-AKI and AKI requiring renal placement therapy. The secondary endpoints included hospitalization time, length of intensive care unit stay, mechanical ventilation time, incidence of short-term adverse events after surgery, hospitalization costs, and renal recovery.
Results: A total of 1974 patients aged from 18 to 80 were enrolled. Among these patients, 1118 (56.6%) were male. The average age was (56.1±12.9) years. The incidence of CSA-AKI was 35.4% in all patients, and the incidence of CSA-AKI in the weekend group was significantly higher than that in the workday group (42.8% vs 34.7%, P=0.038). However, the incidence of AKI-RRT showed no statistically significant difference between the two groups. In AKI-RRT subgroup, there was no statistical difference of the duration from surgery to RRT initiation between the weekend group and the workaday group, nor the urine output at RRT initiation between the workday group and weekend group. The length of hospitalization for AKI patients in the weekend group was significantly shorter than that in workdays (13 [10, 17] days vs. [11, 19] days, P= 0.011). However, no statistical difference was found between weekend group and workday group in terms of short-term adverse events, length of ICU stay, mechanical ventilation duration, or the percentage of complete renal recovery before discharge.
Conclusions: The incidence of CSA-AKI in patients undergoing surgery on weekends was significantly higher than that in workdays, and weekend surgery was an independent risk factor of CSA-AKI. However, the well-organized and performed multidisciplinary teamwork could facilitate to mitigate or rectify the adverse effect of weekend surgery on the short-term prognosis of CSA-AKI patients.

	Workday group(n=628)	Weekend group(n=71)	P value
Death or treatment abandonment[n(%)]	34(5.4%)	4(5.6%)	0.938
Length of hospitalization(d)	14[11,19]	13[10,17]	0.011
Length of ICU stay(d)	2[1,5]	3[2,4]	0.091
Length of ventilation(d)	1[1,2]	1[1,2]	0.988
Renal function recovery[n(%)]			
Total	474(75.5%)	51(71.8%)	
Partial	62(9.9%)	9(12.7%)	
No	92(14.6%)	10(14.1%)	
Time between AKI and total renal recovery(d)	4[2,6]	3[2,5]	0.202
SCr before discharge(umol/L)	99.8±73.1	101.5±77.2	0.856
Hospitalization expenses(1,000RMB)	16.3±7.5	16.7±11.3	0.698

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Epidemiology of Chronic Kidney Disease at One Year Following Pediatric Acute Kidney Injury

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Purpose: It has been shown that adults who experience acute kidney injury (AKI) have a 10 times greater risk of developing end stage renal disease (ESRD) within 12 months in comparison to those who did not experience AKI. Recognition of the AKI characteristics associated with chronic kidney disease (CKD) development by one year holds great potential to reform pediatric AKI follow-up care.

Methods: In this prospective observational study, patients (pts) were enrolled with the onset of severe AKI (sAKI), defined as KDIGO Stage 2-3 for at least 48 hours. Pts agree to follow-up for 5 years after the initial AKI. Serum creatinine (SCr), Cystatin-C, and urine studies are collected at each visit to assess CKD status. For each enrolled pt, days spent in each AKI stage (per KDIGO SCr criteria), AKI etiologies, intensive care unit (ICU) stay, and renal replacement therapy (RRT) requirement were documented. The associations between the described risk factors and the incidence of CKD at 1 year post-AKI (Y1) were observed and subsequent CKD was graded based on glomerular filtration rate (GFR). Statistical significance was determined by either a Fischer's exact or Mann-Whitney test, where appropriate, with a p-value of ≤ 0.05 being considered statistically significant.

Results: A total of 218 pts were enrolled. 19 pts (9%) were deceased at Y1, 1 pt (0.5%) required a kidney transplant prior to Y1, and 130 (60%) had appropriate laboratory studies to assess CKD status at Y1. Of the 130 patients, the SCr of 77 patients (59%) returned to baseline by Y1. In this same population, 4 (3%) developed CKD stage 1, 29 (22%) stage 2, 5 (4%) stage 3, and 4 (3%) stage 4. The most common causes of initial AKI included sepsis or shock, surgery, and nephrotoxic medication exposure (NTMx). AKI characteristics by CKD status at Y1 are displayed in the table below.

Conclusions: There is a significant association between days of AKI, AKI post-surgery, and ICU requirement and CKD at Y1. These findings seem to reinforce the importance of minimizing both days in AKI and in the ICU, as well as reform AKI follow-up care based on patient-specific risk factors, such as surgical procedures.

	CKD (n=42)	No CKD (n=88)	p-value
Days of AKI	13 (11, 24)	11 (7, 18)	0.05
Days of sAKI	9.5 (6, 15)	8 (5, 13)	0.1
AKI post-Surgery	12 (29%)	7 (8%)	0.003
AKI post-Sepsis	7 (17%)	9 (10%)	0.2
AKI post-NTMx	29 (69%)	58 (66%)	0.4
ICU Stay	30 (71%)	44 (50%)	0.02
RRT	15 (36%)	19 (22%)	0.07

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Optimal timing of initiating CRRT in critically ill patients; the value of B-type natriuretic peptide (BNP)

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Purpose
AKI in the ICU is a serious complication can affect the patient outcome, but the appropriate timing of initiating CRRT is controversial. In patients with AKI, volume status is closely connected with prognosis and mortality. The aim of this study was to determine the optimal time for initiating CRRT by evaluating BNP in critically ill patients with AKI

Methods
This was a retrospective, single center (Dong-A university hospital) study, including 246 patients from March 2016 to Feburary 2018.

Results
The mean BNP levels of the 96 patients who died were significantly higher than that of those who survived (2650 versus 920pg/mL; $P<0.05$). The are under curve was 0.97 and optimal thereshold for BNP was 1540pg/mL. Logistic regression analysis demonstrated significant effects on patients survival exerted th level of BNP (odds ratio: 1.050; $P=0.044$)

Conclusions
BNP level more than 1540pg/mL ia an independent marker of mortality in patients with critically ill patients during CRRT.
A large sclaed, prospective study are needed to confirm the vaildation of the optimal threshold of BNP in the critical setting.

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Outcomes After Toxic Alcohol Poisoning: a Systematic Review and Meta-analysis

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Purpose of Study: Although long-recognized to confer morbidity and mortality, little is known regarding short- and long-term outcomes after toxic alcohol poisonings. We sought to comprehensively synthesize existing evidence regarding short- and long-term renal outcomes, mortality and toxin-mediated sequalae after toxic alcohol poisonings amongst adult patients.

Methods: We conducted a literature search in PubMed, MEDLINE, and EMBASE per pre-specified criteria. Any study type that reported the management and clinical outcomes of toxic alcohol poisonings in patients 18 years or older were included. Toxic alcohols of interest included methanol, ethylene glycol (EG), diethylene glycol (DEG), propylene glycol and isopropanol. Citation abstracts were screened and full text articles were

reviewed by two reviewers independently. Data were extracted and quality assessments were performed with validated tools.

Results: 1120 citations were identified, 66 studies (13 retrospective observational study, 1 prospective observational study, 52 case reports/series) met inclusion criteria (total n=2347). In general, included studies had small sample sizes and were of low quality. The indications for renal replacement therapy (RRT) initiation were not reported in majority of observational studies. The pooled in-hospital mortality amongst patients with methanol and EG intoxication were 24% (17-33%, p<0.001) and 11% (5-21%, p<0.001), respectively. Female gender (p=0.006), age (p=0.007) and recent publication year (p=0.014) were associated with lower short-term mortality due to EG intoxication. These variables were not statistically significant amongst the methanol studies. Hemodialysis was the most frequently employed RRT modality. 64.7% to 96.3% of patients with EG poisoning achieved renal recovery and 5.6% to 52.9% had residual renal impairment at hospital discharge. Post-discharge mortality and long-term renal outcomes were seldom reported.

Conclusions: Our review uncovered that there is a paucity of high-quality evidence regarding long-term outcomes after toxic alcohol poisonings. While evidence-based guidelines for clinical management exist for some types of toxic alcohol poisoning, there still may be wide variation in how toxic alcohol poisonings are managed. Despite being a familiar medical problem, a better understanding of short- and long-term outcomes could inform the optimal initial management and longterm follow up of patients with toxic alcohol intoxications.

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Predictors of Mortality Among Leptospirosis Patients with Renal Involvement: A Single Center Experience in the Philippines

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ABSTRACT
Background. Leptospirosis is a zoonosis transmitted through contact with water or soil contaminated by urine from animal reservoirs. Large outbreaks are often associated with increased rainfall and flooding which presumably increased the risk of exposure to contaminated water. The clinical spectrum of leptospirosis varies from mild to severe, or even life-threatening. Up to 10% of Leptospirosis infections may induce acute kidney injury (AKI) and is associated with significant morbidity and mortality. Early evaluation of disease severity might be useful in improving prognosis.
Objective. This study aimed to determine the significant predictors of mortality among leptospirosis patients with renal involvement.
Materials and Methods. A retrospective cohort design was employed through review of records of leptospirosis patients with renal involvement admitted in National Kidney and Transplant Institute (NKTI) from January 2013 to December 2018. Baseline characteristics were extracted and compared among those who survived or died. Logistic regression was employed to determine the significant predictors.
Results. A total of 751 cases were included in this study, 622 survived with renal recovery while 2 survived but remained dialysis dependent upon discharge. The was 16.9% (95% CI: 14.2%-19.6%) mortality among leptospirosis patients with renal involvement. Multivariate analysis showed that diabetes (OR=3.00, 95%CI: 1.53-5.88), jaundice (OR=1.99, 95%CI: 1.09-3.63), oliguria (OR=2.26, 95%CI: 1.26-4.03), anuria (OR=2.57

95%CI: 1.08-6.10), and the need for non-invasive (OR=3.95, 95%CI: 2.16-7.22) and invasive (OR=34.47, 95%CI: 15.92-74.62) respiratory support were significant independent predictors of mortality. Patients who required mechanical ventilation had a mortality of 81.7%.
Conclusion. Identification of significant predictors may help in initiating aggressive therapy to impact survival.

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Community acquired acute kidney disease: Rationale and design of a real-world retrospective cohort study

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OBJECTIVES: Very little data to date have evaluated community-acquired acute renal disease (CA-AKD). Given that there is believed to be a large number of CA-AKD cases, early diagnostic and therapeutic strategies are needed. Characterizing the frequency and prognosis in existing cases is the first step. We sought to identify and characterize a patient cohort with CA-AKD, and to document its impact on renal function and patient mortality.
METHODS: The current study for CA-AKD was performed based on the community electronic health data of residents in Xicheng District of Beijing (serving a population of 421,572). The study population included all adult residents of Xicheng District with at least 2 serum creatinine (sCr) measurements obtained between January, 2010 and November, 2019. Patients who were identified by physician claims or records for dialysis were excluded from the cohort. Pairwise comparisons of sCr measurements were performed in each resident. Patients with an increase or decrease in sCr by 26.5μmol/L or more, or an increase or decrease in sCr of 50% within 3 months were classified as having AKD. For patients who had repeated sCr measurements with intervals longer than 3 months, we expanded the screening criteria of AKD to an increase or decrease in sCr for 1 year. Chronic kidney disease (CKD) was defined as sustained eGFR less than 60 mL/min/1.73 m2 or albuminuria on a least 2 measurements separated by more than 3 months. No kidney disease (NKD) was defined if eGFR was greater than or equal to 60 mL/min/1.73 m2, albuminuria was absent or not measured. The final classification included 4 categories: (1) NKD, (2) AKD, (3) CKD without AKD, (4) CKD with AKD. The least square method was performed and the absolute value of the slope was used as the progression rate of renal dysfunction.
RESULTS: The primary outcome was all-cause mortality. Secondary outcomes included rates of dialysis, the progression rate of renal dysfunction, cardiovascular events and hospitalization rate. Time from the first sCr measurement to each of the outcomes was determined and plotted using cumulative incidence curves. Outcomes of patients with AKD and CKD were examined relative to patients with NKD using Cox proportional hazards regression.
CONCLUSIONS: We describe the study design, eligibility criteria, outcomes and analysis considerations.

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Study of factors affects to combination of extracorporeal membrane oxygenation and continuous renal replacement therapy for patients with acute kidney injury in intensive care unit

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Introduction: Extracorporeal membrane oxygenation (ECMO) is used in critically ill patients who are presenting acute cardiac dysfunction or pulmonary dysfunction such as acute respiratory distress syndrome (ARDS). Some patients suffer from multi organ failure and adapted continuous renal replacement therapy (CRRT) for acute kidney injury. Patients with multi organ failure benefit from ECMO and CRRT, but their treatments are difficult because of their bad sates.
Aim: To investigate the prognostic factors that predict the survival in ICU who required CRRT during ECMO.
Method: Retrospective human observational study
From April 2015 to March 2018, 42 consecutive patients suffered from acute kidney injury under life supporting with ECMO in intensive care unit, Iizuka Hospital. We categorize the patients into two groups: patients who survived and died while in ICU. We compared age, acute physiology and chronic health disease classification system II (APACHE II score), simplified asute physiology score II (SAPS II score) and sequential organ failure assessment score (SOFA score). Continuous data are expressed as median and interquartile 25-75% range. To compare the two group, we performed Mann-Whitney U test. The significance level was fixed at $p < 0.05$.
Resut: 42 patients (female 13, 31.0%) were treated with CRRT and ECMO during the period. Twelve cases each of heart failure, ARDS, septic shock was the cause of ECMO indication. The number of survival group in ICU was 24, death group was 18. The age of survival group vs death group in ICU was 67 [60-73] vs 66 [60-73] (Median [interquartile 25-75% range], respectively) and p value was 0.68. APACHE II score of survival group vs death group in ICU was 31 [27-35] vs 40 [32-45] (Median [interquartile 25-75% range], respectively) and p value < 0.05. SAPS II score of survival group vs death group in ICU was 68 [61-82] vs 85 [73-96] (Median [interquartile 25-75% range], respectively) and p value < 0.05. SOFA score of survival group vs death group in ICU was 9 [7-11] vs 12 [8-15] (Median [interquartile 25-75% range], respectively) and p value was 0.067. The number of hemorrhagic complications during the treatment in survival group and in death group was 7 and 9.
Conclusion: APACHE II score and SAPS II score are associated with the prognosis in the patients treating with ECMO and CRRT in ICU.

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PERSEVERE Biomarkers Predict Severe Acute Kidney Injury and Renal Recovery in Children with Septic Shock

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Purpose: Acute kidney injury (AKI) is a common complication of sepsis that is associated with substantial morbidity and mortality and lacks definitive disease-modifying therapy. As such, early and reliable identification of at risk patients is important for targeted implementation of renal protective measures. Hypothesis: PERSEVERE-II─ a validated, biomarker-based tool for estimating baseline mortality in pediatric septic shock─ can predict the development of severe SA-AKI on day 3 of septic shock (severe D3 SA-AKI).

Methods: We performed a secondary analysis of a prospective study of children admitted to 14 pediatric intensive care units from 2015 to 2018 with septic shock. PERSVERE-II mortality probability was assessed by biomarkers collected in the first 24 hours. The primary outcome was the presence of severe D3 SA-AKI (≥ KDIGO Stage 2). Secondary outcomes included renal recovery by day 3 (defined as improvement in AKI stage) from early SA-AKI (day 1-2, n=130), and the need for renal replacement therapy (RRT). Classification and Regression Tree (CART) analysis was also used to derive a model estimating the probability of severe D3 SA-AKI.

Results: Among 379 patients, 65 (17%) developed severe D3 SA-AKI. Increasing PERSEVERE-II mortality probability was independently associated with increased odds of severe D3 SA-AKI, after adjustment for age and illness severity (OR 1.4, 95% CI: 1.2-1.7, $p<0.001$). Similar associations were found between increasing PERSEVERE-II mortality probability and the need for renal replacement therapy (OR 1.6, 95% CI: 1.3-2, $p<0.001$). Lower PERSEVERE-II mortality probability was independently associated with increased odds of renal recovery among patients with early SA-AKI (OR 1.3, 95% CI: 1.0-1.6, $p<0.047$). A newly derived model incorporating the PERSEVERE biomarkers (specifically, interleukin-8, granzyme B and heat shock protein 70kDa 1B) and day 1 AKI stage predicted severe D3 SA-AKI with an AUROC of 0.95 (95% CI: 0.92 to 0.98) and a positive likelihood ratio of 8.5 (95% CI: 6.2-11.8).

Conclusions: Among children with septic shock, PERSEVERE-II and the PERSEVERE biomarkers predict severe D3 SA-AKI and identify patients with early SA-AKI likely to have renal recovery. Risk stratification of patients using this strategy may allow for proactive intervention in patients at high risk for SA-AKI, potentially mitigating its progression.

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Early Albumin Infusion is Associated with a Shorter Hospital Stay in Patients Hospitalized with Sepsis who Develop Significant Acute Kidney Injury: Real-World Evidence in the United States

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Purpose: The incidence of sepsis and the number of sepsis-related deaths are increasing. Acute kidney injury (AKI) is a common complication in critically ill patients with sepsis/septic shock and is associated with worse outcomes. In ex-US studies, albumin is shown to be effective in the management of circulatory dysfunction in sepsis. In this study, we aimed to examine the impact of albumin infusion on the hospital length of stay (LOS) for septic AKI patients.

Methods: We used a nationwide Electronic Health Record data set (Cerner Health Facts) to examine real-world data on adult patients (>=18 years old) with sepsis/septic shock, admitted between January 1, 2013, and April 30, 2018, identified by International Classification of Disease (ICD-9/10) codes, and receipt of antibiotics. We reported significant AKI as stage 3 based on the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, excluding patients with history of end-stage renal disease or chronic kidney disease stage 5. We calculated the Charlson Comorbidity Index (CCI) and the Acute Physiology Score (APS) at baseline using laboratory data. Generalized linear models were implemented to assess the relationship between albumin and hospital LOS, especially accounting for timing of albumin infusion.

Results: We identified 1,421 unique visits for survivor patients with sepsis/septic shock and AKI stage 3 that met the inclusion criteria. Albumin was infused within 24 hours of admission ('early albumin') in 15%, after 24 hours ('late albumin') in 20%, and not administered in 65%. Both CCI and APS were higher, at presentation, in early albumin cases than late- or no-albumin cases (mean: 7.08 and 7.07, and 58.70 and 43.73, respectively). Unadjusted LOS was lower in patients receiving early albumin as compared to late- or no-albumin (12.94 days versus 13.41 days). A risk-adjusted analysis demonstrated a 7.01% reduction in LOS (95% CI 0.28% - 13.29%, $p = 0.0416$) in patients who received early albumin.

Conclusion: These results show that early albumin infusion was associated with a shorter hospital stay for patients with sepsis/septic shock who develop significant AKI, which may reduce the cost of hospitalization for critically ill patients. Further research is being conducted to assess additional benefits of early albumin administration in this patient population.

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Volume Overload and Mortality Among Patients with Acute Kidney Injury on Extracorporeal Membrane Oxygenation

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Purpose of the Study

Acute kidney injury (AKI) is a frequent complication in patients requiring extracorporeal membrane oxygenation (ECMO) and is associated with increased risk for inpatient morbidity and mortality. We hypothesized that volume overload, defined as greater than 10% increase in body weight, is a potential factor mediating the risk in those with AKI including those requiring renal replacement therapy (AKI-D). We performed a single-center retrospective cohort study to elucidate the impact of AKI, AKI-D, and volume overload on mortality in adults on ECMO.

Methods Used

We performed chart review for all patients who were cannulated on veno-arterial and veno-venous (VA and VV) ECMO from January 2015 to March 2017. Patients with end stage renal disease (ESRD) and those who were on ECMO for less than 24 hours were excluded. Baseline demographics and biochemical parameters were collected. AKI was defined by the KDIGO criteria. Primary outcomes collected were 30 and 90 day all-cause mortality. Secondary outcomes included duration of ECMO and dialysis therapy, duration of admission, dialysis independence at 90 days, and 7 day cumulative volume status.

Results

We found 117 patients on ECMO during the study period but excluded 19. Of the 98 remaining patients, 83 developed AKI (85%) and 48 developed AKI-D (49%) all of whom received CRRT. Separately, 33 (34%) developed volume overload (weight gain > 10% of baseline weight), of whom 19 (58%) developed AKI-D. Patients with AKI-D were heavier on admission, more likely to have CAD, less likely to be on ACEi/ARB, and were on greater number of vasoactives at the time of ECMO ($p<0.05$ for all). In Kaplan Meier analysis (Figure 1), 90 day mortality was highest in patients with AKI-D and volume overload (82%), similar between those with AKI-D and no volume overload when compared to those with volume overload without AKI-D (60%), and lowest for patients without volume overload and no AKI-D (34%). In multivariate regression analysis, volume overload remained an independent predictor of 90 day mortality when adjusting for AKI and AKI-D (OR 2.9, 95% CI 1.1-7.6, $p=0.03$).

Conclusions

Volume overload has significant prognostic value in patients treated with ECMO. Despite our limited numbers, initiating RRT in this critically ill population may help to control the deleterious effects of volume overload.

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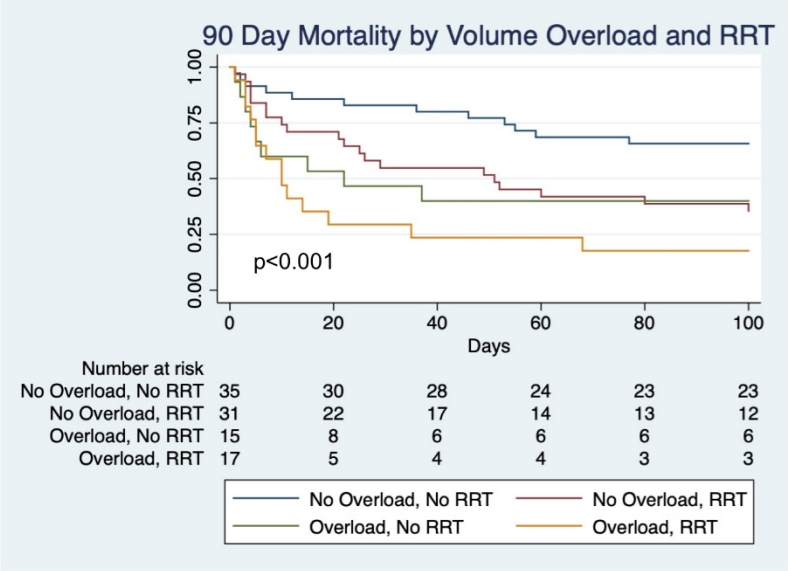

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Epidemiology of Acute Kidney Injury in Neonatal Cardiac Surgery without Cardiopulmonary Bypass: A Report from the NEPHRON Collaborative

Katja M Gist[1], Jun Sasaki[2], Saidie Rodriguez[3], Santiago Borasino[4], David Selewski[5], Kristal Hock[4], Jeffrey Alten[6]

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Introduction: Neonatal and Pediatric Heart and Renal Outcomes Network (NEPHRON) is a multicenter collaborative created to better understand cardiac surgery induced acute kidney injury (CS-AKI). The purpose of this study was to describe the epidemiology, center variation and outcomes associated with neonatal CS-AKI utilizing the modified Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine and urine output criteria in neonates who underwent cardiac surgery without cardiopulmonary bypass (CPB).

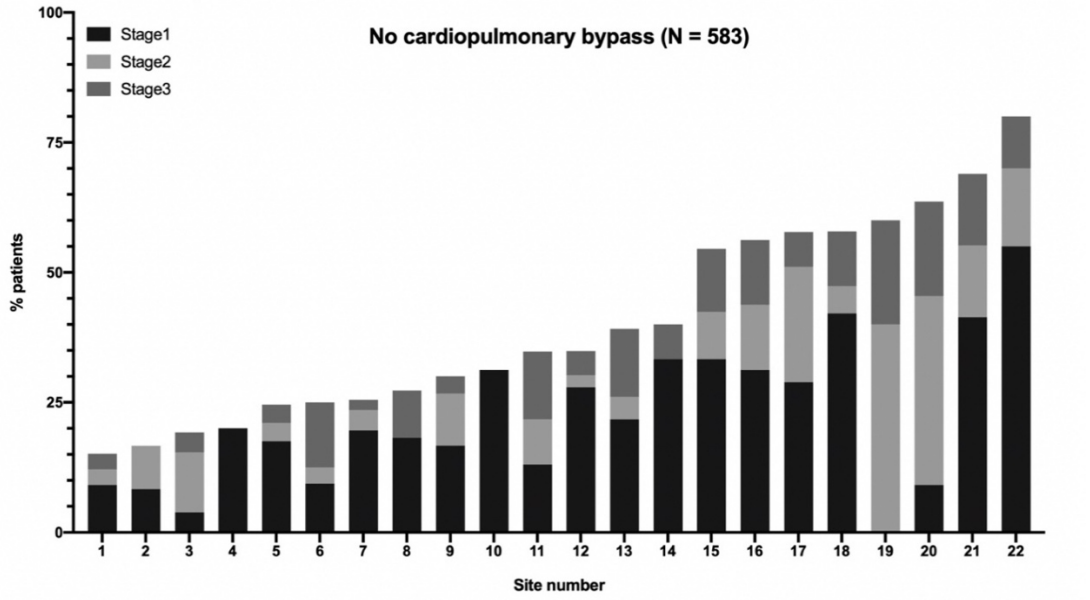
Methods: 22 center study of neonates (<30 days) who underwent cardiac surgery without CPB. Data was extracted utilizing the CS-AKI module combined with the Pediatric Cardiac Critical Care Consortium data set. Consecutive retrospective subjects were screened for enrollment starting 8/2017. CS-AKI data was collected for 6 postoperative days (POD). Exclusions: preoperative AKI and ECMO and reoperation.

Results: 583 underwent cardiac surgery without CPB. Any stage CS-AKI occurred in 38% (n=224), with severe CS-AKI (stage 2 or 3) occurring in 15.6% (n=91). CS-AKI occurred most commonly on post-operative day 1 (32%), with decreasing prevalence by day 6 (Table 1). CS-AKI prevalence and severity varied significantly

between centers (Figure 1). Lower creatinine prior to surgery and longer cross clamp duration were associated with AKI. No other demographic and operative characteristics differed between those with vs. without AKI. There was no difference in outcomes in patients with vs. without AKI.

Conclusions: When defined by the modified KDIGO serum creatinine or urine output criteria, CS-AKI occurs in more than a third of patients. Longer cross clamp duration was associated with CS-AKI. Prevalence and severity of CS-AKI varied significantly across centers but there was no association of any CS-AKI with outcomes.

Figure 1. Center variation in cardiac surgery associated acute kidney injury prevalence and severity



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Epidemiology of Acute Kidney Injury in Neonatal Cardiac Surgery: A Report from the NEPHRON Collaborative

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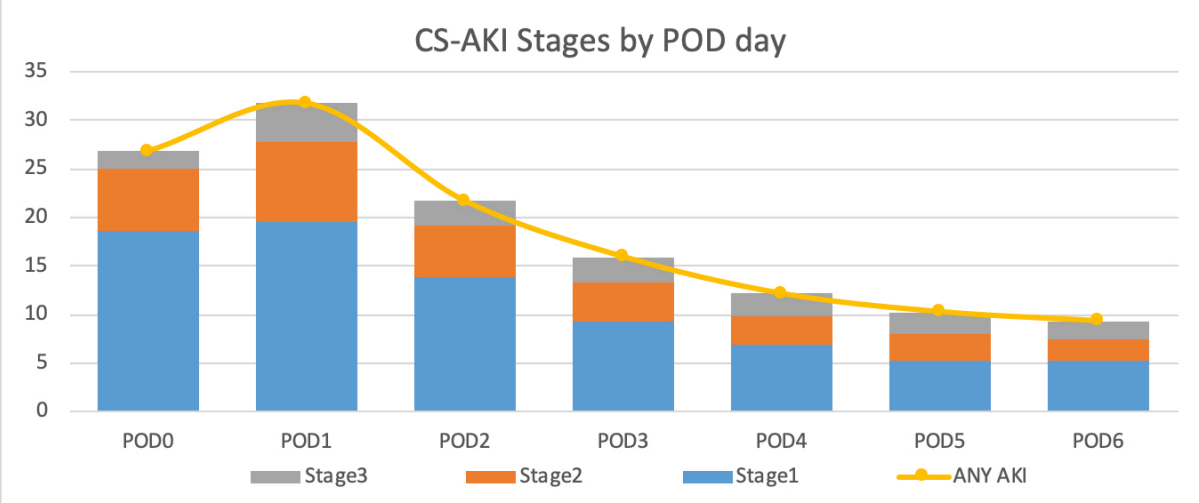
Introduction: Neonatal and Pediatric Heart and Renal Outcomes Network (NEPHRON) is a multicenter collaborative created to better understand cardiac surgery induced acute kidney injury (CS-AKI). NEPHRON's first aim was to describe the multicenter epidemiology & outcomes associated with neonatal CS-AKI, utilizing modified Kidney Disease: Improving Global Outcomes (KDIGO) criteria with both urine output (UOP) and serum creatinine criteria.

Methods: 22-center study of neonates (≤30 days) undergoing cardiac surgery utilizing a CS-AKI module combined with the Pediatric Cardiac Critical Care Consortium data set. Consecutive retrospective subjects were screened for enrollment starting 8/2017. CS-AKI data was collected for 6 postoperative days (POD). Exclusions: preoperative AKI, ECMO, and reoperation. Primary outcome: hospital mortality. Multinomial regression determined CS-AKI predictors. Associations among CS-AKI stages and mortality and other outcomes were assessed with multivariable logistic or linear regression.

Results: 2240 neonates were included. CS-AKI occurred in 1207 (54%). Only 312 (26%) met both creatinine and UOP criteria for CS-AKI; 412 (35%) met only creatinine criteria and 462 (38%) met only UOP criteria. CS-AKI rate peaked on POD 1, with 9.3% having CS-AKI on POD 6 [Figure 1]. Center CS-AKI rates varied >3 fold across the three centers: 27% to 86%; site-specific proportions of KDIGO stages also widely varied – including stage 3. KDIGO Stage 3 was most commonly defined by oligo-anuria, 65% vs. 35% by creatinine criteria. Only KDIGO Stage 3 was associated with mortality: [OR 2.4; 95% CI 1.3-4.6]. No stage of CS-AKI was associated with increased duration of mechanical ventilation or hospital length of stay. In multivariate analysis, only use of cardiopulmonary bypass (CPB), but not CPB duration, increased the odds of CS-AKI [OR 1.5; 95% CI 1.0-2.3]. After controlling for institutional practice variation, no other patient or treatment level variables were independently associated with development of CS-AKI.
Conclusions: When defined by KDIGO, CS-AKI occurs in >50% of neonatal cardiac surgeries; rates and severity vary widely by center. CS-AKI did not importantly impact most outcomes; only KDIGO stage 3 is independently associated with mortality. Further NEPHRON analyses will explore center variation, CS-AKI risk factors, understanding impact of oligo-anuria, and optimizing the definition of neonatal CS-AKI.



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Variation in Degree and Timing of Cumulative Fluid Overload Following Neonatal Cardiac Surgery

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INTRODUCTION
Fluid overload after cardiac surgery may worsen outcomes. However, features of fluid balance (FB) such as degree and timing have not been described. The multi-center NEonatal and Pediatric Heart Renal Outcomes Network (NEPHRON) was developed to investigate acute kidney injury (AKI) after cardiac surgery and as such collected daily FB. We sought to use NEPHRON to describe degree and timing of FB among neonates after cardiac surgery.

METHODS
We analyzed data from all neonatal patients undergoing cardiac surgery at 22 NEPHRON sites collected between August 2017 to January 2018. Exclusions included: operation in the preceding 7 days, preoperative renal replacement or serum creatinine >1.5 mg/dL, and need for perioperative (<24 hours) extracorporeal support. Cumulative FB (CFB) was assessed from the time of ICU admission until postoperative day (POD) 6 and was defined as:

CFB% = [(sum of all preceding daily net FB) / preoperative weight] x 100.

RESULTS
A total of 2223 patients (1652 cardiopulmonary bypass (CPB) and 571 non-CPB) were included. Overall intensive care unit mortality was 3.1% (n=69). The median peak CFB% for those with CPB was 4.6% (0.2-10) compared to 5.4% (1-11) for non-CPB. 26% (n=581) of all patients had a >10% peak CFB%. Overall, peak CFB% occurred on POD 1 in 44% (n=981) of patients and on POD 6 in 32% (n=702) of patients. Among patients undergoing CPB, peak CFB% occurred most often on POD 1 (49%, n=803) and the nadir occurred most often on POD 6 (23%, n=87). Among non-CPB patients peak CFB% occurred most often on POD 6 (42%, n=241) and the nadir most often occurred on POD 1 (23%, n= 134). There was substantial variation in center level degree, timing, and duration of CFB%. Peak CFB% for surgical complexity categories 1-5 (5 denoting greater complexity) respectively was 8.2% (2.5-14.5), 5.4% (0.9-11.9), 4.6% (0.1-10.2), 4.9% (0.6-10.5), and 3.7% (-0.8-8.2). Figure 1 summarizes the multivariable model of FB candidate variables with mortality, duration of mechanical ventilation and length of stay.

CONCLUSIONS
26% of subjects had a peak CFB% >10% and it most often occurred early in those with CPB and late in non-CPB. Variation in timing, degree and duration of CFB% exists across centers. Future analyses are needed to understand the clinical implications of variation in these features of FB in neonatal cardiac surgery.

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	* Adjusted logistic regression modeling (n=2214)			
Fluid Balance (FB) Candidates	Mortality	Duration of ventilation	*CICU LOS*	*Hospital LOS*
Time to 1st negative daily FB	NS	**IRR = 1.14 ; p = 0.001**	**IRR = 1.13; p = 0.005**	**IRR = 1.10; p = 0.016**
Cumulative FB% POD 1	NS	NS	NS	NS
Peak Cumulative FB% continuous	NS	NS	NS	NS
Peak Cumulative FB% categorical	NS	NS	NS	NS
<10%				NS
10 to <20%				
20 to <30%				
>30%				
Interactions of FB% with Time to 1st negative daily FB	NS	NS	NS	NS

*Adjusted for underweight, pre-term, chromosomal abnormalities, pre-operative ventilation, pre-operative mechanic support , [1]pre-operative high risk factors, [2]'Other' preoperative risk factors, STAT score, pre-operative VIS score, CT output, any post-op complication, and any post-operative infection. ([1] 'Pre-operative high risk factors' included cardio-pulmonary resuscitation, shock at time of surgery, hepatic dysfunction, stroke, cerebrovascular accident, intracranial hemorrhage >grade 2 within 48h prior to surgery, or renal failure requiring dialysis. [2] 'Other pre-operative risk factors' were any STS risk factor for the index operation other than those included in 'high risk' and invasive ventilation to treat cardiorespiratory failure and pre- operative mechanical support.)

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Long term outcomes of acute kidney injury to/on chronic kidney disease in Thailand.

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Background
Acute kidney injury (AKI) has been increasingly recognized as a major risk factor for adverse long-term outcomes such as chronic kidney disease (CKD), end-stage renal disease (ESRD), and death. There are several pathophysiologic mechanisms by which AKI can lead to CKD including changes in renal vasculature, glomerulosclerosis, tubular atrophy, and interstitial fibrosis. However, the epidemiology of long-term outcomes of AKI has not been well-established, especially in low-and middle income countries. Our primary aim is to explore the long-term outcomes, namely 2-year mortality and 2-year CKD progression, of AKI to/on CKD in Thailand.

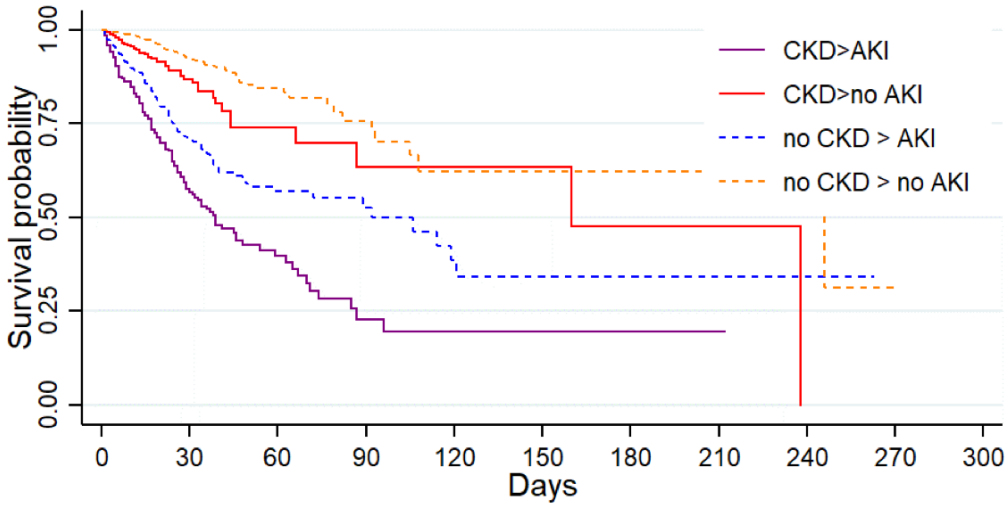
Methods
This is a retrospective study from King Chulalongkorn Memorial Hospital, Bangkok, Thailand. We included all patients who were hospitalized during 2017 and had 3-month baseline serum creatinine level. Patients who did not have any creatinine measurement during hospitalization and those with history of ESRD were excluded from this study. AKI and CKD were defined by using KDIGO criteria. Participants were divided into 4 groups based on their AKI and CKD status. CKD progression is defined by having at least one more stage from the baseline CKD status at two year.

Results
Of 12,718 patients from the entire database, a total of 9,802 patients were included in the analysis. Twenty-nine percent of the patients had evidence of CKD prior to hospitalization. AKI was detected in 8.8% of hospitalization. Hospital mortality of each groups were between 2.0% to 40.8%. Two-year mortality of AKI on CKD patients was 37.8% compared to 27.1% of those CKD patients without AKI (P=0.002). While, 2-year mortality was 32% in patients with AKI alone and 20.7% for patients without any CKD or AKI (P<0.001). In

patients without CKD, those with AKI had more new-onset CKD at two years than those without AKI (13% vs 8% respectively, P<0.001). In CKD patients, 2-year CKD progression occurs more frequently in patients with AKI (29.1% vs 18.2%, P=0.007).

Conclusion

Patients with AKI, especially those with CKD, are at higher risk of adverse long-term clinical consequences. However, further multicenter prospective study is suggested to improve the understanding of long-term outcomes of AKI to/on CKD patients.



Number at risk

CKD>AKI	319	83	24	7	3	3	2	1	0	0	0
CKD>no AKI	2247	95	20	10	6	5	2	1	0	0	0
no CKD > AKI	541	128	42	20	10	6	3	2	2	0	0
no CKD > no AKI	6678	373	75	29	10	8	6	5	3	1	0

Multivariable Cox proportional hazard model:
adjusted for age and DM,HT,DLP,IHD,CHF,CVD,CANCER,FRACTION comorbidity
CKD > AKI: aHR (95% CI) = 8.1 (6.2 - 10.5), p<0.001
CKD > noAKI: aHR (95% CI) = 2.3 (1.7 - 3.0), p<0.001
no CKD > AKI: aHR (95% CI) = 4.0 (3.1 - 5.1), p<0.001
no CKD > no AKI: Reference

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CLINICAL PROFILE OF AKI

Mayur Patil[1], Rechal Shah[1], Jaydeep Hirpara[1]

[1]*IKDRC,* [2]*CIMS,* [3]*IKDRC*

Background: Acute Kidney Injury (AKI), is a very common entity affecting patients suffering from a wide variety of illnesses. Many patients remain dialysis dependant or are left with partial renal impairment. Even patients who have complete recovery of renal function are at increased risk of CKD in future. Since ARF is creditable and because of personal interest in providing total cure of the issue, I have selected to study its clinical profile and variables affecting its outcome.

Methods: Adults with ARF admitted to the nephrology department during August 2017 to December 2019 were studied. KDIGO criteria was used to define AKI. Patients were subjected to renal biopsy and hemodialysis as and when required. Patients who became dialysis independent with good renal function were discharged and followed fortnightly for 3 months, monthly for six months.

Results: Most of patients (40.90%) were from 14-35 years age group. Second peak was seen in 56-65 years. Incidence of Intrinsic ARF was higher than Prerenal and Postrenal ARF. Main etiologies were malaria 12.38%, pregnancy related AKI 9.99%, gasteroenteritis 9.99%, infections 23.80%, multiple myeloma 8.57%. Glomerulonephritis was seen in 21.90% of cases & most common amongst it was PIGN (21.73%). There were 17.39% of AKI due to crescentic GN. Out of which 50% were pauci immune & 37.5% were immune complex GN & one case (12.5%) of anti GBM disease. Dialysis was done in 70.47% of patients, 29.52% of patients were kept on conservative management. Complete recovery was seen in 51.42% of cases, partial recovery in 17.61% of cases & 60% of patients became dialysis independent. Patients presented with oliguric ARF were 140/210, i.e. 66.67%. Survival was better in non-oliguric ARF (85.71%) than oliguric ARF (72.85%). Overall survival in our study was seen in 76.19% of cases out of which 23.45% progressed to end stage renal disease.

Conclusion: Acute renal failure is very rewarding and creditable in general because most of the causes are reversible. Timely specific treatment for some of the etiologies is very important to prevent progression to permanent renal insufficiency.

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CLINICAL PROFILE OF PREGNANCY RELATED AKI (PRAKI): A SINGLE CENTER EXPERIENCE

Mayur Patil[1], Jaydeep Hirpara[1]

[1]*IKDRC*

BACKGROUND
Acute renal failure (ARF) of obstetric origin is one of the most common complication of pregnancy and leads to poor maternal and fetal outcome. The incidence of PRAKI in developed country is 1 in 20,000 pregnancies, where as in developing country like India is 1 in 50. Septic abortion, poor follow up of pregnancy, limited screening of pregnant patients with hypertensive complications and late referrals to tertiary center are responsible for high incidence of ARF in developing countries.
METHODS
The study was conducted at government aided tertiary care hospital between April 2018 to March 2019. A total 1021 patients of ARF were admitted out of which 96 were PRAKI. ARF was defined according to KIDIGO guidelines. Renal biopsy was performed if the patient was oliguric or creatinine still >2mg/dl at the end of three weeks.
RESULTS
The incidence of PRAKI was 9.4%. Most common age group was 24-29 years(53.13%). 45.83% patients presented in late pregnancy while 36.46% presented in postpartum period. Antenatal care was recieved by only 30.21% patients. 25% patients required termination of pregnancy. Most common cause for PRAKI was puerperal sepsis followed by pre eclampsia. 18.75% patients were managed conservatively while 69.79% were kept on intermittent hemodialysis and 11.46% required SLED/CRRT. Acute patchy cortical necrosis was most common histological finding, others were thrombotic microangiopathy and glomerulonephritis. Complete recovery occured in 43.75%, whereas 16.67% had partial recovery (became dialysis independent but with persistent renal impairment), 19.79% were kept on renal replacement therapy. Maternal mortality was seen in 19.79% of cases.
CONCLUSION
In our study, puerperal sepsis was the most common etiological factor for pregnancy-related AKI. Sepsis, thrombocytopenia, disseminated intra-vascular coagulation were associated with increased mortality.

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Renal Recovery After Continuous Renal Replacement Therapy during Extracorporeal Membrane Oxygenation

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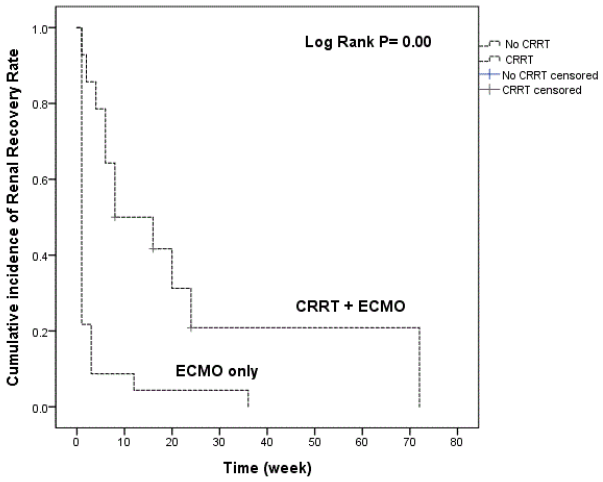
Concomitant use of continuous renal replacement therapy (CRRT) during extracorporeal membrane oxygenation (ECMO) may limit patients to spontaneous renal recovery and expose them to wasteful medical expense and unnecessary trauma of vascular procedure, and complications of CRRT. There has been many

studies regarding on the effect on CRRT on mortality in ECMO patients. However, the renal outcome after CRRT on ECMO has been poorly understood especially in adult patients.
The aim of the study is firstly to evaluate the significance of CRRT in ECMO patients and secondly to confirm the renal outcome among these patient population.
63 survivors after receiving ECMO treatment from Jan 2009 to August 2019 were retrospectively reviewed. 37 patients developed AKI according to kidney disease improving global outcomes (KDIGO) classification, 37% of whom (n= 14) received CRRT treatment. They were followed up with median duration of 379 days (104-379) to analyze their renal recovery (eGFR greater than 60mL/min/1.73m2). To evaluate the factors associated with renal recovery, the patients who recovered with eGFR up to 60mL/min/1.73m2 within 3 month after AKI development were compared with those who did not.
Among 37 patients with AKI, 17 patients (46%) and 20 patients (54%) belonged to stage 1-2 and stage 3, respectively. Compared with patients on CRRT and ECMO, patients on ECMO alone showed higher renal recovery rate ($p<0.05$). 1.5 year was the longest time required to renal recovery. The noticeable finding was that none of the cases needed dialysis in long term except the three patients who was lost in follow up after the discharge, although time takes longer to renal recovery in patients on CRRT and ECMO than in patients on ECMO alone. In univariable analysis, Sequential organ failure assessment (SOFA), Simplified acute physiology score (SAPS 2),
Acute physiologic assessment and chronic health evaluation (APACHE 2) score were found as factors affecting renal recovery (OR 1.812, 1.060, 1.153, respectively, $P<0.05$). However, after adjustment with confounding variables, APACHE 2 score was found only statistically relevant (OR 1.153, $p<0.05$).
Since the majority of patients recovered renal function after concomitant use of CRRT on ECMO in adult patients, CRRT should not be avoided due to concerns about poor renal outcome. SOFA, SAPS 3, APACHE2 score at the time of ECMO initiation were associated with renal recovery.



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Mortality Associated to the Severity of AKI Using pRIFLE Criteria at Initiation of RRT (in Critically Ill Children)

Stephanie Reynaud[1], Paloma Parvex[1], Serge Grazioli[1]

[1]*Hopitaux Universitaire de Geneve*

Introduction
The high mortality and morbidity in critically ill children treated with renal replacement therapy (RRT) have multifactorial components. To evaluate the association between the severity of acute kidney injury (AKI) at RRT initiation using the pediatric RIFLE criteria (pRIFLE) and the patient outcomes, we undertake a retrospective, observational study in a single Swiss center pediatric intensive care unit (PICU). Data extraction was performed for the first episode of RRT in children admitted to the PICU between 2008 and 2018.
Results
Ninety-four patients required RRT during the study period. Of these, 86.2% presented with AKI according to the pRIFLE criteria at RRT initiation (stage “R” (risk) 8.6%, stage “I” (injury) 13.6%, and stage “F”(failure) 77.8%). When assessing the duration in stage “F” before RRT initiation, we found that 27% of children spent less than 24h, 21.3% between 28-48h, 8.5% between 48-72h, and 9.5% more than 72h.
Overall mortality was 45.7% with 3 children (3%) requiring chronic RRT. The distribution of patients according to the pRIFLE critera was similar among survivors and non-survivors with a majority of children in the stage “F”(69% in the non-survivor and 64% in survivors groups). Time spent in stage “F”, had no effect on mortality; 57% in children with more than 24h and 50% in children with less than 24h in stage “F”. There was also no difference in PICU lengths of stay, duration of mechanical ventilation, and duration of RRT according to the pRIFLE criteria at RRT initiation. In multivariable logistic regression analysis, non-surgical cardiac disease (odd ratio, 16.73; 95%CI 1.6-174.387), an elevated PELOD score at RRT initiation (odd ratio, 1.076; 95%CI 1.031-1.124) and elevated fluid balance at RRT initiation (odd ratio, 1.006; 95%CI 1.001-1.012) were associated with an increase odds of mortality.
Conclusion
In this cohort of PICU pediatric patients requiring RRT, the majority presented with stage “F” of the pRIFLE criteria. The severity of AKI according to the pRIFLE or the duration at “F” stage before RRT initiation didn’t predict mortality or morbidity. An elevated PELOD score, a diagnosis of a non-surgical cardiac disease or an elevated fluid balance were associated with increased mortality.

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Association of Fluid Balance with All-Cause and Cause-Specific Mortality in Critically Ill Adult Patients Receiving Continuous Renal Replacement Therapy.

Keisuke Okamoto[1], Blaithin A McMahon[1]

[1]*Medical University of South Carolina*

Purpose of the study
Continuous renal replacement therapy (CRRT) is commonly used for the management of fluid balance and/or electrolytes disturbances in the setting of critically ill patients in intensive care unit (ICU). A recent study showed greater net ultrafiltration (UF) rate is associated with lower survival among critically ill patients with acute kidney injury (AKI). The purpose of this study is to assess an association between daily fluid balance in critically ill patients with severe (AKI) receiving CRRT and mortality. More specifically, linking fluid status, net ultrafiltration (UF) and cause-specific mortality.

Methods
We consecutively evaluated 41 patients with severe AKI-requiring CRRT who were admitted to the medical ICU at Medical University of South Carolina (MUSC) between 1/1/2019 to 7/31/2019. We stratified patients into 3 categories according to the median daily net fluid balance while the patients were receiving CRRT, and assessed 28-day all-cause and cause-specific mortality among these 3 groups. Group A (a net negative daily fluid balance) median of -1065 [-3710 to -687] ml per day, Group B (a net even to slightly negative daily fluid balance) median of -202 [-521 to 300] ml per day), and Group C (a net positive daily fluid balance) +1252 [337 to 7093] ml per day). The net ultrafiltration rate as per each group A-C was assessed. Finally, the exact cause of death was established with each patient.

Results
Group A consisted of 14 patients, Group B consisted of 13 patients and Group C consisted of 14 patients. Among the 41 patients, 19 (46.3%) patients had a 28-day mortality. Group C, the net positive daily fluid balance group, was associated with the highest mortality rate of 71.4% (10 out of 14 patients died) but did not appear to die from a predominant volume-related illness (cardiogenic failure or hypoxic respiratory failure). When compared to group A and group B, the 28-day mortality was 28.6% ($P< 0.01$) and 38.5% ($P<0.05$), respectively. There was no statistically significant difference between the net UF rate or among the three groups.

Conclusion
Positive daily net fluid balance and not net UF rate on CRRT predicted worse 28-day survival rate compared with negative or intermediate daily net fluid balance. Further research into the cause-specific mortality of volume overloaded patients on CRRT is required.

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Hospital Discharge Kidney Dysfunction and Treatment with Anti-Hypertensive Medications After Pediatric Extracorporeal Membrane Oxygenation

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Introduction: Acute kidney injury(AKI) is frequent in children treated with extracorporeal membrane oxygenation(ECMO) and associated with mortality and morbidity. AKI may incur risk for long-term chronic kidney disease(CKD). Recovery from AKI may be associated with long-term CKD risk.
Objectives: In children treated with ECMO, determine a)prevalence of hospital discharge kidney dysfunction (DischKidDysf: discharge serum creatinine[SCr] ≥1.5Xpre-ECMO baseline) and need for anti-hypertensive medication (DischHTNmeds); b)associations between AKI on ECMO, and other factors (e.g. ECMO duration, ECMO indication, age, oxygenation index) with DischKidDysf and DischHTNmeds.
Methods: 6-center retrospective cohort study (Kidney Injury During Membrane Oxygenation cohort) of children (<18 yrs old) on ECMO≥24 hrs from 2007-11. Exposure: AKI (SCr criteria of the KDIGO definition) during ECMO, defined as a) any AKI (yes/no) and ≥Stage 2 AKI (yes/no), regardless of renal replacement therapy[RRT]; b) AKI and ≥Stage 2 AKI, including RRT as an AKI criterion. Outcomes: as in objectives. Analyses: Univariable analyses comparing AKI and clinical factors between patients with vs. without outcomes.
Results: N=345 included (median[IQR] age 25 days(2-457); 61.2%(216/354) VA ECMO; 38.8%(137/354) VV ECMO; ECMO indication pulmonary(62.1%), cardiac(20.9%), ECPR(17%); 197(55.6%) AKI and 126(35.6%) ≥Stage 2 AKI, disregarding RRT; 234(66.1%) AKI and 189(53.4%) ≥Stage 2 AKI, including RRT as an AKI criterion). N=43(12.1%) had DischKidDysf; 115(33.3%) had DischHTNmeds. Patients with DischKidDysf were significantly more likely to have AKI on ECMO (any AKI: 95.4% vs. 50.2, p<0.0001), regardless of AKI definition. Similarly, patients with DischHTNmeds were more likely to have AKI on ECMO (any AKI: 72.2% vs. 48.1%, p<0.0001). Older age, oxygenation index, non-renal complications, ECMO indication, and center were all associated with DischKidDysf and with DischHTNmeds (all p≤0.01). Fewer ECMO hours was associated with DischKidDysf (p=0.03); VA ECMO mode was more common in patients with DischHTNmeds (80.9% vs. 52.2%, p=0.001).
Conclusion:
DischKidDysf and DischHTNmeds are common after pediatric ECMO, suggesting that kidney health follow-up should be considered in ECMO survivors. Discharge kidney outcomes are associated with AKI on ECMO and patient/treatment/illness severity factors. Future work will determine if the relation of AKI with discharge kidney outcomes is independent of these factors.

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Prevalence of Proteinuria, Abnormal GFR, and Return-to-Baseline Serum Creatinine at One Year Following Severe Acute Kidney Injury

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Purpose: Recent studies have shown that children who experience acute kidney injury are at a greater risk of developing chronic kidney disease. Identifying those at the greatest risk for progression, and therefore requiring more frequent follow-up, is less clear.
Methods: Patients with severe AKI (sAKI) were approached for consent to participate in this 5-year prospective observational cohort study for follow-up assessment. Prevalence of proteinuria, abnormal GFR (Cystatin-C or eGFR), and return to baseline of serum creatinine (rbSCr) at 3, 6, and 12 months are presented for patients with no CKD or Stage I CKD (Group 1) and Stages II-IV CKD (Group 2) at one year following sAKI.
Results: A total of 37 (30%) patients had Stage II-IV at one year following sAKI. The remaining 85 patients had either Stage I CKD (n=4) or no evidence of CKD (n=85). Those in Group 2 had higher rates of proteinuria at 3 months (100%) compared to those in Group 1 (61%). At 6 months post sAKI, 58% of those in Group I had proteinuria, whereas rates in Group 2 were slightly higher (67%). At one year post sAKI, both Group I (62%) and Group II (64%) had similar rates of proteinuria. Overall, return to baseline SCr rates remained fairly stable within each group, however, some differences were observed between Group I and 2. At one year post sAKI, only 46% of those in Group 2 achieved a return-to-baseline SCr, compared to those in Group 1 (80%). Only 9% of patients in Group 1 had an abnormal GFR at year 1, compared to those in Group 2 (100%).
Conclusion: This data supports the important role of proteinuria and abnormal GFR as important markers of kidney damage. Future research is needed to define specific risk-stratification categories to determine which patients may be at the greatest risk for progression, and therefore, frequency of follow-up.

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ACUTE KIDNEY INJURY AFTER PROCEDURES OF ORTHOTOPIC LIVER TRANSPLANTATION: RISK FACTORS, RENAL OUTCOMES AND SURVIVAL.

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Introduction.
The incidence of acute renal injury (AKI) after orthotopic liver transplantation (OLT) ranges between 40 and 70%. The etiology of this syndrome is multifactorial.
Methods
Medical records of patients undergoing OLT in the period from January 2012 to August 2019 were reviewed. A total of 355 patients were included, of which 171 patients presented AKI. Baseline characteristics, variables during surgery and variables during their stay in intensive were analyzed. Renal outcomes and survival were also analyzed.
Results
In the group without AKI age mean was 45.8 years and 37% were men, in the group with AKI the age mean was 51.2 years and 54% were men (P = 0.001). Mean baseline creatinine was 0.77 while vs 0.88 mg/dl P = 0.003. Furosemide prior to transplantation was found: 51.6% vs 71.9% P = 0.001. A difference was also found between the incidence of AKI and the number of AKI events in the 3 months prior to transplantation (17.3% vs

37.4% P = 0.001) and (0.21 vs. 0.53)
During surgery. Difference was found in maximum lactate, maximum dose of norepinephrine and vasopressin use during surgery: (5.1 vs. 5.8 P = 0.014), (0.59 vs 0.34 P = 0.001), (36% vs 51% P = 0.003)
Differences were also found in drained ascites and anehepatic period: (1508 vs 973 SD vs 1871 P = 0.021) and (52.9 vs 57.4 P = 0.014).
In the stay in the ICU, there was a difference in the income of liquids first and second 8 hours after transplant (1319 vs 1984 P = 0.001) and (1208 vs 1606 P = 0.009), norepinephrine dose in the first 24 hours (0.14 vs 0.27 P = 0.001), use of vancomycin and anidulafungin (27.1% vs. 42.1% P = 0.02) and (3.8% vs. 13.4% P = 0.001), transfusion of blood derivatives 33.15% vs 59% (P = 0.001).
There was also a difference in creatinine and GFR at the end of hospitalization (0.67 vs 0.97 P = 0.001) and (104 vs 82.6 P = 0.001).
Survival at 7 days after the transplant 100% vs 96.5% P = 0.01. Survival 30 days 99.5% vs 93.6% P = 0.002.
Conclusions
The incidence of AKI in the first 7 days was 48%, which is consistent with that reported in the world literature. The development of AKI seems to be multifactorial influencing baseline characteristics of patients before transplantation and renal insults during surgery and intensive care stay. As reported in other series, AKI was associated with higher mortality at 7 and 30 days, in addition to lower GFR at patient discharge and higher risk of CKD.

Variable	Group without AKI	Group with AKI	P value
Age (years)	45.8 SD 12	51.2 SD 10.77	0.001
Male (%)	37	54	0.001
Baseline creatinine (mg/dl	0.77 mg/dl SD 0.36	0.88 mg/dl SD 0.36	0.003
Furosemide prior OLT (%)	51.6	71.9	0.001
Incidence AKI last 3 months (%)	17.3	34.7%	0.001
Number of AKI events	0.21 SD 0.38	0.53 SD 0.83	0.001
Maximum lactate in surgery	5.1 SD 2.08	5.8 SD 3.4	0.014
Dose norepinephrine surgery (gammas)	0.59 SD 0.73	0.34 SD 0.26	0.001
Vasopressin use during surgery (%)	36	51	0.003
Drained ascites in surgery (ml)	1508 SD 2453	973 SD vs 1871	0.021
Anehepatic period (min)	52.9 SD 10.3	57.4 SD 22.4	0.014
income of liquids in the first 8 h (ml)	1319 SD 1217	1984 SD 1736	0.001
ncome of liquids in the second 8 h (ml)	1208 SD 1061	1606 SD 1344	0.009
Norepinephrine dose in ICU (gammas)	0.14 SD 0.14	0.27 SD 0.23	0.001
Surgical reintervention (%)	2.7	9.9	0.05
Vancomycin in ICU (%)	27.1	42.1	0.02
Anidulafungin (%)	3.8	13.4	0.001
Transfusions in ICU (%)	33.1	59	0.001
Fresh frozen plasmas (units)	0.57 SD 1.07	0.29 SD 0.77	0.05
Number of days in the ICU	3.92 SD 4	5.7 SD 6.8	0.002
Creatinine end of hospitalization	0.67 SD 0.21	0.97 SD 0.46	0.001
GFR at the end of hospitalization	104 SD 21.05	82.6 SD 28.58	0.001
30 day survival (%)	95.5	93.6%	0.002

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Acute Kidney Disease and Long-Term Outcomes

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Background: Acute kidney injury (AKI) with early reversal was associated with good prognosis in both short- and long-term. In contrast, little is known about long-term impacts of persistent form of AKI.

Methods: We retrospectively analyzed a total of 1,322 patients with any stage of AKI in King Chulalongkorn Memorial Hospital from November 2015 to October 2017. We classified AKI by duration into three categories according to ADQI consensus (rapid reversal AKI, 2 days; persistent AKI, 3-7 days; and acute kidney disease (AKD), >7 days). After excluded missing AKI data, 1,255 patients remained in the analyses. Survival analyses were performed comparing 1-year outcomes among these AKI groups.

Results: Of these, 121 (9.6%) patients died within the first 7 days, 279 (22.2%) patients had rapid reversal of AKI, 284 (22.6%) patients had persistent AKI, and 571 (45.4%) patients were classified as AKD. Median age was 68 (IQR, 56-80) years with male predominant (55.1%). Persistent AKI and AKD groups had significant higher rate of pre-existing CKD (48.6% and 48.9%) compared to rapid reversal group (30.8%) (Table 1). About 56% of patients who developed AKD suffered from severe AKI. AKD group was associated with the highest urinary NGAL level at AKI diagnosis. Compared to rapid reversal AKI, AKD had adjusted HR of 2.09 (95% CI, 1.65-2.65; p <0.001) for death at 1 year; 2.92 (95% CI, 2.35-3.64; p <0.001) for MAKE365; and 4.23 (95% CI, 2.85-6.27; p <0.001) for dialysis at 1 year.

Conclusion: AKD was not uncommon and was associated with adverse outcomes on dialysis and mortality at 1 year.

see table on following page

Table 1. Demographic data

Variable	Rapid reversal AKI (n=279)	Persistent AKI (n=284)	AKD (n=571)	Early Death (n=121)	P value
Age	66 (55-80)	70 (56-81)	68 (56-80)	65 (54-77)	0.028
Male sex	157 (56.3)	152 (53.5)	310 (54.3)	72 (59.5)	0.673
CKD	86 (30.8)	138 (48.6)	279 (48.9)	30 (24.8)	<0.001
DM	103 (36.9)	114 (40.1)	211 (37.0)	35 (28.9)	0.205
HTN	149 (53.4)	150 (52.8)	309 (54.1)	52 (43.0)	0.165
CHF	30 (10.8)	29 (10.2)	40 (7.0)	9 (7.4)	0.201
Chronic liver disease	42 (15.1)	50 (17.6)	78 (13.7)	26 (21.5)	0.125
Baseline SCr	1.24 (0.92-1.69)	1.56 (1.10-2.37)	1.79 (1.12-2.96)	1.17 (0.82-2.01)	<0.001
Baseline eGFR	56.5 (39.7-73.9)	42.2 (26.8-65.2)	38.4 (23.4-65.8)	60.9 (39.8-90.2)	<0.001
SCr at AKI diagnosis	1.90 (1.50-2.58)	2.38 (1.77-3.40)	2.90 (2.01-4.33)	2.11 (1.58-2.82)	<0.001
Urine NGAL at AKI diagnosis	102 (72-200)	203 (96-630)	599 (108-1900)	1159 (188-3650)	<0.001
Maximum AKI stage					
Stage 1	167 (59.9)	109 (38.4)	139 (24.3)	28 (23.1)	<0.001
Stage 2	72 (25.8)	73 (25.7)	110 (19.3)	24 (19.8)	0.061
Stage 3	40 (14.3)	102 (35.9)	322 (56.4)	69 (57.0)	<0.001

Data shown as number (%) or Median (IQR).

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Meropenem Dosing Recommendations For Thai Critically Ill Patients Receiving Continuous Renal Replacement Therapy

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Antibiotic dosing in critically ill patients undergoing continuous renal replacement therapy (CRRT) is still a challenge. Meropenem is one of the most common carbapenems used to manage infections in the intensive care unit. Its pharmacokinetics (PK) are small molecular weight (437.52 Da), very low plasma protein binding (2%), and low volume of distribution (15-20 L). Therefore, meropenem is conveniently removed via CRRT. Unfortunately, recommendations of meropenem dosing regimens mostly are suggested from published PK studies of the Western literatures. Differences in PK of various populations such as body weights and non-renal clearance may contribute to the need for dosing adaptation. This study aimed to define meropenem dosing recommendations from pharmacokinetic data of Thai critically ill patients including acute kidney injury receiving CRRT. Mathematical pharmacokinetic models were developed using published demographic/PK data in Thai critically ill patients with known variability. Bodyweight used in the models was extracted from a database of Asian critically ill patients. CRRT modalities (predilution continuous venovenous hemofiltration, CVVH ,and continuous venovenous hemodialysis, CVVHD) with different effluent rates were modeled. Meropenem regimens from available clinical resources were evaluated on the probability of target attainment (PTA) using pharmacodynamics (PD) target of the amount of time in which free meropenem concentration that exceeds the 4 times minimum inhibitory concentration (MIC) of Pseudomonas aeruginosa for the initial 48 hour-therapy. At least 40% of a dosing interval (40% fT>4MIC) and MIC breakpoint of 2 mg/L were applied in the models. Optimal regimens were defined from regimens that yielded a PTA ≥ 90% with the smallest total dose. Each regimen was tested in a group of different 5,000 virtual patients. Our results showed that the optimal meropenem dosing regimen of 750 mg every 8 hours is recommended for patients receiving both CRRT modalities with 3 different effluent rates of 20, 25 and 35 mL/kg/h. Some of the literature-based dosing regimens cannot attain the PK/PD targets. While some regimens were considered as supratherapeutic doses in Thai critically ill patients receiving CRRT and may cause meropenem toxicity in high-risk patients. Dosing adaptation in various populations is crucial from our study. Clinical validation of the finding is definitely needed.

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The LAPIS Trial: A Biomarker-guided Implementation of Kidney-Sparing Care Measures to Prevent Acute Kidney Injury in Sepsis Patients

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Background
Sepsis associated acute kidney injury (SA-AKI) increases the risk of morbidity and mortality. A novel biomarker [TIMP-2/IGFBP-7] (NephroCheck®) is available to aid in the clinical evaluation of critically ill patients who are at increased risk for developing AKI.

Subjects and methods
LAPIS is a randomized, controlled, multicenter trial of adults with a clinical diagnosis of sepsis at risk of developing AKI. Sites in the USA and Europe will participate to the study, enrolling approximately 540 subjects.

Enrollment and testing:
Subjects will be randomized 1:1 into 1 of 2 arms:
Control arm: subjects will be assessed for AKI based on clinical criteria and standard of care (SOC) assessments. NephroCheck testing will be performed with results masked to the site.
Intervention arm: subjects will be assessed for AKI based on clinical criteria plus three NephroCheck tests during the first day following the clinical diagnosis of sepsis.

Patient management:
Subjects randomized to the Control arm will be treated according to the attending clinician's clinical judgment and the site's SOC for treating sepsis patients; all interventions will be recorded.

Subjects randomized to the Intervention arm will be treated based on test results:
Subjects with all three negative NephroCheck Test results will receive a Test Negative Sepsis Bundle (TNSB) which allows for less intensive monitoring and faster de-escalation of care than SOC.
Subjects with any positive NephroCheck Test result will receive a Kidney-Sparing Sepsis Bundle (KSSB) with 3 levels of care possible depending on the test results. Interventions are based upon the KDIGO Guidelines.

The primary endpoint will be a composite of death, dialysis (defined as any form of renal replacement therapy) or progression of 2 or more stages of AKI (stage 0 to stage 2/3 and stage 1 to stage 3) within 72 hours. We will assess the impact of the NephroCheck-guided KSSB and TNSB on AKI severity healthcare utilization. Additional endpoints will include hospital and ICU length of stay, 30-day readmission rates and other health-economic endpoints. The study is scheduled to begin enrollment in early 2020.

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Survival comparison between CVVHDF and CVVH in Septic acute kidney injury.

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Background
The mortality of the septic acute kidney injury (AKI) is still high, despite of improvement in renal replacement technology. It was reported that adding a dialysis dose to continuous veno-venous hemofiltration (CVVH) increased their survival. By the way, hemofiltration is more proper for clearance of inflammatory mediators than hemodialysis in sepsis. We tested whether continuous veno-venous hemodiafiltration (CVVHDF) is really better than CVVH at the same net effluent according to their body weight in the intensive care unit (ICU) patients with septic AKI.
Methods
CVVHDF was performed by Prismaflex (©Baxter International) with blood flow rate (BFR) 150ml/min at the dialysate flow rate 20ml/kg/hour, in addition to the replacement fluid flow rate 20ml/kg/hour. In contrast, replacement fluid flow rate of CVVH was 40ml/kg/hour. Patient's removal rate was individually adjusted by attending staff considering clinical status.
Results
In this prospective randomized pilot study, 100 patients were assigned to CVVH (n=47, M:F=25:22, age 64±15 years) or CVVHDF (n=49, M:F=30:19, age 65±11 years). There was no difference in baseline characteristics such as age, sex, body weight, serum creatinine, blood urea nitrogen (BUN), beta-2 microglobulin, Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) score between two groups. However, there was no significant difference of reduction ratio in serum creatinine, BUN, beta-2 microglobulin, APACHE II and SOFA score between two groups. Seven, Twenty-eight, and sixty days survivals were no statistically significant differences between two groups
Conclusions
In conclusion, none of CVVH and CVVHDF was better than the other mode in clearance of waste products and survival at the same net effluent in this study. In the future, large scaled randomized prospective study will be necessary to distinguish better one from the other to give greater survival change to the critically ill patient with septic AKI.

Table 3. Outcomes by treatment groups

	CVVHDF group	CVVHF group	p
Total CRRT days	8.5±8.9	7.4±8.0	0.57
Total ICU days	15.8±18.2	15.8±15.5	0.99
Renal recovery at hospital discharge(%)	31	20	0.29
Survival (%)			
7 days	67	70	0.82
28 days	47	45	1.00
60 days	31	25	0.64

CRRT, continous renal replacement therapy; CVVHDF, continous veno-venous hemodiafiltration; CVVHF, continous veno-venous hemofiltration; ICU, intensive care unit.

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The Renal Angina Index Fails to Identify Patients with Subclinical Acute Kidney Injury

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Purpose: Subclinical acute kidney injury (AKI)─ a state of tubular injury biomarker positivity in the absence of serum creatinine (Cr) rise─ is a well described entity associated with worse clinical outcomes. We previously reported a 20% incidence of subclinical AKI in patients admitted to a pediatric intensive care unit (PICU). However, a knowledge gap exists in identifying high risk patients to screen with kidney injury biomarkers to detect subclinical AKI. The renal angina index (RAI) is a validated tool predicting severe AKI in critically ill children and identifies a high-risk subset of patients. We hypothesized urinary neutrophil gelatinase-associated lipocalin (uNGAL) testing for patients fulfilling renal angina criteria (RAI+) would allow identification of patients with subclinical AKI, while simultaneously reducing testing in low-risk patients.

Methods: We analyzed data from a prospective, observational cohort of children admitted to the PICU from May 2017 to October 2019 who were RAI+ (RAI≥8) with uNGAL and Cr samples collected on admission. uNGAL+ was defined as ≥150 ng/ml. Cr changes from baseline were assessed using the KDIGO criteria. Patients with subclinical AKI (uNGAL+/Cr-) were identified and compared to patients without biomarker elevation (uNGAL-/Cr-). Demographic data were compared, including receipt of nephrotoxins. Outcome data including severity of AKI and the presence of fluid overload (FO, defined as >10% FO) at day 3 were assessed.

Results: We included 141 patients in this cohort (53.2% male, median age 10.3 years, mortality 9.2%). Seven patients (5%) had subclinical AKI on the day of PICU admission. When compared to uNGAL-/Cr- patients (n=36), patients with subclinical AKI received higher numbers of nephrotoxins, both on day of admission (2 [1,2] vs. 1 [1,1], p=0.010), and for the first 7 days of PICU stay (2 [1,2] vs. 1 [1,1.8], p=0.026). These patients were more likely to have FO at day 3 (OR 12.5, 1.9-80.2, p=0.008), and had a trend towards increased risk for AKI at day 3 (OR 14, 1.1-184, p=0.064).

Conclusion: Subclinical AKI appears to be associated with worse outcomes in patients fulfilling renal angina criteria. However, the incidence of subclinical AKI in this cohort is low, suggesting the RAI is an inadequate screening tool for identifying this subset of patients. Further study is needed to identify patients who may benefit from testing for subclinical AKI, including examining the role of nephrotoxins.

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Proenkephalin Predicts Renal Dysfunction, Organ Failures, Renal Replacement Therapy, and Mortality in Sepsis

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Introduction: Kidney failure occurs frequently in sepsis and is associated with high mortality. Proenkephalin (PENK) is an emerging plasma biomarker for renal function, and has been investigated so far mainly in Europe and North America. We evaluated whether PENK level could predict severity, organ failure, and 30-day mortality in a Korean cohort of septic patients.

Methods: In a total of 215 septic patients, PENK level was measured using the sphingotest® penKid® assay (Sphingotec GmbH, Hennigsdorf, Germany). The PENK levels were analyzed in terms of sequential (sepsis-related) organ failure assessment (SOFA) renal subscore, the Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate (CKD-EPI eGFR) categories, requirement of renal replacement therapy (RRT), sepsis severity, vasopressor use, and 30-day mortality. The number of organ failures, SOFA subscores, requiring RRT, and 30-day mortality were compared according to the PENK quartiles.

Results: The PENK levels were significantly associated with SOFA renal subscore and CKD-EPI eGFR categories (all $P < 0.0001$). The PENK levels were significantly higher in patients who required RRT than in those who did not require RRT ($P < 0.0001$). The PENK levels were significantly higher in patients with septic shock, vasopressor use, and non-survivors than in patients with solitary sepsis, no vasopressor use, and survivors, respectively (all $P < 0.01$). The PENK quartiles were associated with the number of organ failures as well as SOFA renal, cardiovascular, respiratory, and central nervous system subscores (all $P < 0.05$). High PENK level was also associated with high 30-day mortality ($P < 0.0001$).

Conclusions: PENK is a useful and objective marker to predict renal dysfunction, severity, organ failure, and 30-day mortality in septic patients. Data gained in our Korean patient cohort are comparable to those reported for non-Asian populations.

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Efficacy of rasburicase in children with acute kidney injury from diarrhea associated hemolytic uremic syndrome

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Background: Diarrhea associated hemolytic uremic syndrome (D+HUS) is a common etiology of acute kidney injury (AKI) in children. Hyperuricemia during acute phase is a typical finding of D+HUS. Recently we have used rasburicase to manage hyperuricemia, thereby ameliorate AKI and accelerate their recovery. Here we assessed the efficacy of rasburicase in D+HUS.
Methods: We retrospectively analyzed the medical records of pediatric D+HUS patients who were admitted to Seoul National University Children's Hospital between January 2001 and July 2017. We compared the clinical outcomes between those treated with rasburicase (rasburicase group) and the rest (control group).
Results: A total of 72 patients were analyzed. Their median age was 3.2 years old. Median values of the lowest hemoglobin, the lowest platelet, and the highest uric acid were 6.3g/dL, 24,000/uL, and 12.6mg/dL, respectively. Twelve (16.7%) were treated with rasburicase. It was administered once at a median dose of 0.10 (range 0.05–0.20) mg/kg during the first day of admission. There was no difference in age, sex, the lowest hemoglobin, the lowest estimated glomerular filtration rate (eGFR), and the highest uric acid between the rasburicase group and the control group. The lowest platelet in rasburicase group was lower than that in the control group (14,000 vs. 25,000/uL; P=0.002). In the rasburicase group, hyperuricemia was rapidly reversed (2.4 vs. 6.5 days; P<0.001). There was no statistical difference in requirement of dialysis (66.7% vs. 55.0%; P=0.456) and the duration of dialysis (5.5 vs. 8.6 days; P=0.262) between the two groups. However, median hospital length of stay was shorter in the rasburicase group than in the control group (12.9 vs. 18.2 days; P=0.043), and median eGFR at 1 year follow up was lower in the control group than in the rasburicase group (81.2 vs. 111.0 mL/min/1.73m2, P=0.002).
Conclusion: Although rasburicase treatment in patients with D+HUS did not lower the requirement of dialysis, patients who were treated with rasburicase during the acute phase were discharged earlier from the hospital and had better renal function at 1 year follow-up. Since there are no known effective therapies for AKI induced by D+HUS, we may consider rasburicase to improve their long-term renal outcome.

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Urinary Aquaporin 2 Predict Acute Kidney Injury in Congestive Heart Failure Patients

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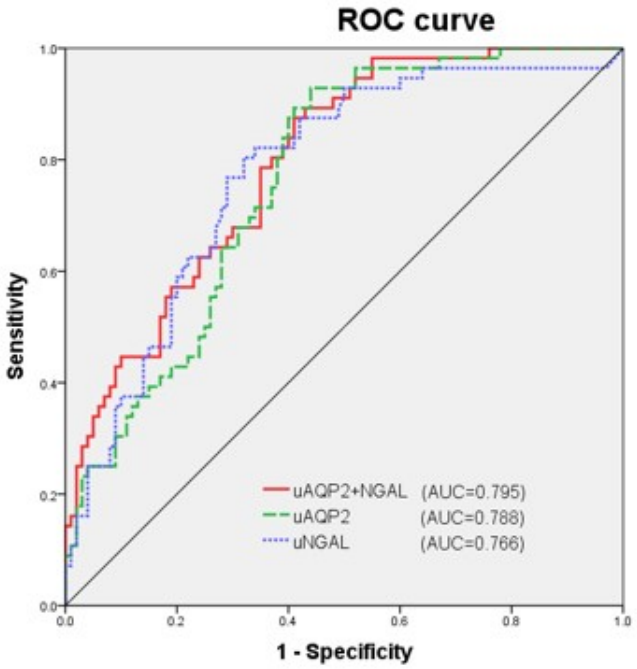
Background: Acute kidney injury (AKI) is associated is frequently encountered in congestive heart failure (CHF) patients with increased morbidity and mortality. Early detection of urinary biomarker reflect kidney injury might provide the chance for prompt diagnosis and improve outcome. Urinary aquaporin 2 (uAQP2) is upregulated in the CHF and reported associated renal injury in several clinical context. This study aims to investigate whether uAQP2 could to predict AKI in CHF patients.
Methods: This was a prospective observational study conducted in a coronary care unit (CCU) of a tertiary care university hospital in Taiwan. Patients admitted to CCU with CHF were enrolled. Serum and urinary samples of the enrolled patients collected between November 2009 and November 2014. The definition of AKI was based on KDIGO classification. Urine Neutrophil gelatinase-associated lipocalin (uNGAL) was used to compare the discriminative power with uAQP2. All prospective demographic, clinical, and laboratory data were evaluated as predictors of AKI.
Results: A total of 189 adult patients with a mean age of 68 years were investigated. AKI was diagnosed in 69 (36.5%) patients. For discriminating AKI, both normalized uNGAL and uAQP2 demonstrated acceptable areas under the receiver operating characteristic curve (AUROC) (0.776 and 0.788 respectively). A combination of these two markers revealed an AUROC of 0.795.
Conclusion: Our result revealed that uAQP2 is a considerable biomarker for AKI in CHF patients in CCU. In addition, combination of uAQP2 and uNAGL have better discriminating power for predicting AKI in CHF patients than uAQP2 or uNAGL alone.



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Validation of the Advanced Chronic Kidney Disease after Acute Kidney Injury Risk Index

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BACKGROUND
Acute kidney injury (AKI) is common among hospitalized patients and is known to increase the risk of developing chronic kidney. A model by James, M. et al. was devised to predict advance chronic kidney disease following acute kidney injury and would identify aim to identify these patients who are at risk. This study validated the prediction tool in the Filipino population.

METHOD
The study is a single-center retrospective validation cohort study and included 186 adult patients who were admitted at St. Luke's Medical Center-Quezon City and had been referred to or admitted by Nephrology service for management of acute kidney injury. The discriminative ability of the predictive model of James, M. et. al., to predict the outcome chronic kidney disease was evaluated using the area under the receiver operating characteristic curve (AUC).

RESULTS
The predictive model had an acceptable predictive ability for chronic kidney disease after AKI with an AUC of 0.75. Based on the study, it has a sensitivity of 75% and specificity of 70.67%.

CONCLUSION
The prediction model devised by James M. et al to predict advanced chronic kidney disease following acute kidney injury has a fair diagnostic accuracy and may still be used by clinicians to tailor their follow ups to their patients.

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Fluid Accumulation in Critically Ill Children

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Objectives:
To describe the characteristics of fluid accumulation in critically ill children and evaluate the association between the degree, timing and rate of fluid accumulation with patient outcomes and use of health services.

Design:
Retrospective cohort study involving all children admitted to PICU in Alberta, Canada between January 1, 2015, and December 31, 2015.

Results:
A total of 1,017 patients were included. Fluid overload% (FO%) increased from median (IQR) 1.58% (0.23-

3.56; n=1017) on day 1 to 16.42% (7.53-27.34; n=111) on day 10 among those remaining in PICU. The median (IQR) peak FO% was 5.85% (2.63-11.02). The proportion (95% CI) of patients with peak FO% >10% and >20% was 32.7% (29.8-35.7) and 9.1% (7.4-11.1), respectively. Younger patients, those with higher PIM3 score, a primary shock diagnosis, who developed AKI, and who received non-invasive, invasive ventilation, or inotropic support had significantly higher peak FO%.

Thirty-two children (3.1%) died in PICU. Peak FO% was significantly associated with greater PICU mortality. For each 1% increase in peak FO%, there was a 5% increase in odds of mortality [adjusted odds ratio (aOR) 1.05 (95% CI, 1.02 – 1.09); P= 0.001]. PICU mortality for children with a peak FO% >20% was threefold greater compared with those with a peak FO% <20% [aOR 2.97 (95% CI, 1.11 – 7.97); p=0.03]. Fifty-three (5.2%) children developed MAKE30 while in PICU. Greater peak FO% was associated with significantly increased odds of MAKE30 [aOR 1.05 (95% CI, 1.02- 1.08); p=0.001]. On average, for every 1% increase in peak FO%, there was approximately 16 hours increase in length of mechanical ventilation [aOR 0.66 day (95% CI, 0.54- 0.77); p<0.001] and half a day increase in length of PICU stay [aOR 0.52 (95% CI, 0.46- 0.58); p<0.001]. The rate of fluid accumulation was associated with PICU mortality [aOR 1.15 (95% CI, 1.01 – 1.31); P = 0.04], MAKE30 [aOR 1.16 (95% CI, 1.03 – 1.30); P = 0.02], length of mechanical ventilation [B coefficient 0.80 (95% CI, 0.24 – 1.36); P = 0.005], and length of PICU stay [B coefficient 0.38 (95% CI, 0.11 – 0.66); P = 0.007].

Conclusions
Fluid accumulation occurs early during PICU course and is associated with considerable mortality and morbidity. These findings highlight the need for the development and evaluation of interventional strategies to mitigate the potential harm associated with fluid accumulation.

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Urinary Biomarkers and the Progression from Pediatric AKI to CKD

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Purpose: Children with a history of acute kidney injury (AKI) are at an increased risk of developing chronic kidney disease (CKD). Urinary biomarkers, including kidney injury molecule-1 (KIM-1), liver-type fatty acid-binding protein (L-FABP), and neutrophil gelatinase-associated lipocalin (NGAL), have been shown to be increased in AKI, and elevated levels are also associated with worsening CKD. We assessed for an association between urinary biomarker levels with the progression of AKI to CKD.

Methods: Urine collection was integrated into a larger prospective, observational study of pediatric patients with severe AKI (KDIGO Stage 2-3 by serum creatinine criteria), lasting at least 48 hours. Specimen were to be collected at each study visit, if possible, including at time of AKI as well as 14 days (D14), 30 days (M1), 3 months (M3), 6 months (M6), and 1-year (Y1) post AKI. Stored samples were analyzed by ELISA for NGAL, KIM-1, and L-FABP. Biomarker concentrations are described with median and interquartile range values by MAKE365 - major kidney events including death, kidney transplant, or progression to CKD by Y1. Between group comparisons were assessed by Mann-Whitney U test (p-value <0.05 was considered significant), and area under the curve (AUC) was assessed by a receiver operating characteristic (ROC) curve.

Results: 218 patients were enrolled, and 114 (52%) had a urine specimen from at least one study visit. Of those with any urine samples, 33 (29%) had evidence of CKD, 1 (1%) had undergone a kidney transplant, and 12

(11%) were deceased by Y1. Biomarker concentrations at M1 were higher in patients with MAKE365: NGAL 117.7 vs. 14.5 ng/mL (p<0.01); KIM-1 921.3 vs. 581.7 pg/mL(p=0.1); L-FABP 14.3 vs. 2.9 ng/mL (p<0.01). AUC for NGAL at M1 was 0.78 (95% CI 0.65, 0.91) and for L-FABP was 0.79 (0.65, 0.93). In addition, L-FABP was elevated in MAKE365 at the time of AKI (16.9 vs. 4.3, p=0.04) and D14 (31.0 vs. 4.24 vs, p=0.03).

Conclusion: Urinary biomarkers at M1 are elevated in the MAKE365 population, suggesting slow tubular damage at M1 may be a predictor of long-term kidney outcomes. This is a small sample size, and more research is needed.

	MAKE365 at M1 (n=21)	No MAKE at M1 (n=26)	MAKE365 at M3 (n=20)	No MAKE at M3 (n=28)
NGAL	117.7 (37.4, 252.4)	14.5 (3.7, 44.3)	11.6 (3.1, 36.6)	17 (5.3, 53.5)
L-FABP	14.3 (4.3, 66.8)	2.9 (1.6, 4.7)	4.4 (1.7, 15.5)	2.6 (1, 5.2)
KIM-1	921.3 (612, 1982.3)	581.7 (242.5, 1765.4)	619.7 (301.2, 974.8)	583.5 (230.2, 1128.3)

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Kidney Histopathology In Critically Ill Patients With Septic Acute Renal Injury

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Purpose of the study
Acute Kidney Injury (AKI) is frequently observed in critically ill patients. The reported incidence is 30 to 68%. Sepsis is the most frequent etiology (50%) of AKI (S-AKI) in this patient population. Histopathological studies in the context of S-AKI are scarce and the findings found have been minor tubular lesions, leukocyte infiltration and apoptosis with very little necrosis. The nonspecific tubulointerstitial lesions could be described as acute tubular injury (ATI).The purpose of the study is to describe kidney histopathology of patients with S-AKI and correlate the histological findings with the AKI severity, the presence of septic shock and the multiple organic dysfunction (MOD) degree using the SOFA score.
Methods
Prospective, observational and analytical study of a cohort of critically ill patients with S-AKI who died from sepsis at “Hospital Español” Intensive Care Unit (ICU). The kidney necropsies were performed within 2 hours after death. Descriptives values are shown as n (%), mean (±SD) or median (Q1-Q3).
Results
We included twelve patients who died from sepsis between June 2018 and November 2019. Male sex: 8 (66,6%), age: 60.8 (± 15) years, APACHE II score: 28.9 (± 9.53). SOFA score at ICU discharge: 16.2 (± 2.25). ICU stay: 4 (1-10) days. The predominant source of sepsis was respiratory (66.6%). All the patients had septic shock with SOFA cardiovascular score at ICU discharge of 4 (± 0). Creatinine at ICU discharge: 2.92 (± 1.01) mg/dL. All the patients presented AKI stage 3 (KDIGO classification) at the same time. Histopathological findings: tubularinterstitial leukocyte infiltration 11 (91.6%), cast formation 10 (83.3%), loss of nuclei 7 (58.3%), edematous interstitium 6 (50%), loss of brush border 5 (41.6%), vacuolization of tubular cells 5 (41.6%), sloughing of viable tubular cells 4 (33%), loss of epithelial lining 2 (16.6%). Total of patients with ATI: 12 (100%). Necrotic casts 3 (25%), sloughing of necrotic tubular cells 1 (8.3%), tubular necrotic cells 1

(8.3%), coagulative necrosis 1 (8.3%), glomerular involvement 1 (8.3%), vascular necrosis 1 (8.3%), thrombosis 1 (8.3%). Total of patients with necrosis: 4 (33.3%).
Conclusions
The main histopathological findings in postmortem kidney biopsies in deceased septic shock patients with S-AKI KDIGO 3, showed nonspecific tubulointerstitial lesions, or ATI. Tubular necrosis was only observed in one third of the cases.

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Proenkephalin A 119-159 (penKid) - A Novel Biomarker For Acute Kidney Injury In Sepsis: An Observational Study

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Purpose.
Sepsis is a leading cause of death worldwide and poses a major clinical challenge. The kidneys are among the most frequently affected organs in the septic patient, and play an important role in outcome. Serum Creatinine, the established marker for evaluating kidney function, is not optimal for the acute setting due to a delayed onset and significant reliance on non-renal factors. Proenkephalin A 119-159 (penKid) is a surrogate marker for the endogenous opioid peptide enkephalin, has been suggested as a marker of true kidney function and shown to predict both acute and chronic kidney disease. The aim of this prospective observational study was to assess a single measurement of penKid as a predictor of acute kidney injury (AKI), multi-organ failure and mortality in sepsis among unselected patients presenting to the emergency department (ED).

Method.
We enrolled 644 adult patients (18 years and older) consecutively between December 1, 2013 and February 1, 2015. 56 patients were excluded due to incomplete data. We analyzed penKid in 588 plasma samples from patients with sepsis (≥2SIRS criteria + suspected infection) which were drawn at presentation to the ED. Logistic regression analysis was used to relate levels of penKid at presentation to AKI, multi-organ failure, 28-day mortality and progression of renal SOFA subscore. Odds ratios represent the number of standard deviations from the mean of log-transformed penKid concentration.

Results.
Median penKid in patients without AKI was 74 (IQR: 53-101) pmol/L while it was 129 (IQR: 92-178) pmol/L in septic patients with AKI. In logistic regression models adjusted for age and sex, penKid predicted AKI within 48 hours and 7 days, but these associations were attenuated after additional adjustment for creatinine-based estimated glomerular filtration rate (eGFR). In models adjusted for age, sex and eGFR, penKid predicted worsening renal function by incremental renal SOFA subscores as well as multi-organ failure and 28-day mortality. In contrast, eGFR did not predict 28-day mortality.

Conclusion.
PenKid is an effective predictor of renal injury, severe multi-organ failure and mortality, particularly among unselected patients with sepsis and seemingly intact renal function at presentation to the ED.

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Worsening renal function and Proenkephalin A 119-156 (penKid) among patients with rSOFA 0 and ≤ 1.

	per SD from mean of log-transformed penKid		[a]penKid > 100pmol/L	
	[b]No eGFR adjustment	[c]eGFR adjusted	No eGFR adjustment	eGFR adjusted
	[d]rSOFA = 0			
OR	**2.6	1.7	***5.5	*3.2
(95% CI)	(1.4-4.9)	(0.9-3.2)	(2.2-13.9)	(1.1-9.1)
	[e]rSOFA ≤ 1			
OR	***3.6	*2.1	***10.1	*3.7
(95% CI)	(1.9-6.8)	(1.0-4.4)	(3.2-31.7)	(1.0-13.1)

[a]Cutoff of 100 pmol/L has been suggested previously as significantly increased risk for renal deterioration. [b]Logistic regression model adjusted for sex & age. [c]Additional adjustment for eGFR, by Modification of Diet in Renal Disease (MDRD) Study formula. [d]Presenting with an rSOFA score = 0 (intact renal function) and being up-classified to a higher rSOFA category within 48 hours. Observed 29 up-classifications among 359 patients. [e]Presenting with an rSOFA score ≤ 1 (intact and moderately impaired) renal function and being up-classified to an rSOFA category of 2 or higher within 48 hours. Observed 17 up-classification among 447 patients. *p<0.05, **p<0.005, ***p<0.001.

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Cell-Based Therapy using Human Amnion Epithelial Cells in the Treatment of Acute Kidney Injury

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The incidence of acute kidney injury(AKI) is increasing worldwide. Due to multifactorial mechanisms, there is no effective pharmacological therapy to prevent the evolution or reverse the injury once established. An alternative approach with increasing interest is cell-based therapy. Among the multiple proposed cell types, human amnion epithelial cells (hAECs) are promising. These cells are highly abundant, and their use poses no ethical concern. hAECs have been shown to have multiple differentiation potentials of potential stem cells and the immuno-regulatory potential of adult stem cells. In this study, an AKI model through renal ischemia reperfusion injury (IRI) was stablished by clamping bilateral renal pedicles at 37℃for 30-33 minutes, leading to moderate to severe renal damage. hAECs were injected into the tail vein of mice immediately after IRI. At day 1/2/3/7 blood samples and kidney specimens were collected for blood biochemical analysis and renal pathological staining for regeneration and fibrosis. Compared to mesenchymal stem cells (MSCs), injection of hAECs could reduce the seven-day mortality rate from 80% to 47.4% ($p < 0.05$) in the most severe IRI group. Moreover, the serum creatinine level of the injection group was significantly lower than that of the control group on the first day after surgery. We evaluated the protective effect of hAECs injection on kidney after moderate IRI from four aspects: proliferation, apoptosis, immunity and interstitial fibrosis. We found that injection of hAECs increased cell proliferation and decreased cell apoptosis in the kidney; increased the number of M2 type macrophage infiltration and decreased the level of fibrosis. Injection of exosomes isolated from hAECs might have similar or even better effects on renal protection. Further investigation was performed using proteomic analysis to identify factors secreted by hAECs that exert their beneficial effects. Taken together, our work has shown the protective function of hAECs and its exosomes on the treatment of AKI in IRI animal model. Hopefully, this research will assist in designing future clinical trials and may lead to the development of an antifibrotic therapy based on the hAEC exosomes.

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The Safety and Efficacy on the Systemic Inflammatory Response and Renal Function of Human Chorionic Gonadotropin Hormone-Derivative EA-230 on On-Pump Cardiac Surgery Patients, a Randomized Double-Blin

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Background
Cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response and is associated with acute kidney injury (AKI). Pregnancy is associated with immunotolerance and an increased glomerular filtration rate (GFR). EA-230, a tetrapeptide derived from the human chorionic gonadotropin hormone, has shown to be well tolerated and to exert immunomodulatory and renoprotective effects in animals. This study investigates the safety, tolerability, immunomodulatory and renoprotective effects of EA-230 in cardiac surgery patients.

Methods
In a prospective, double-blind, placebo-controlled, randomized study with an adaptive design, 180 patients undergoing elective cardiac surgery using CPB received either 90 mg/kg/hour EA-230 or placebo during surgery. In this safety study, the primary efficacy endpoint was the modulation of plasma IL-6 concentrations by EA-230. Secondary, the focus was on kidney function, using plasma clearance of iohexol (GFRiohexol), creatinine-based estimated GFR (eGFRmdrd) and the incidence of AKI (RIFLE criteria). Other endpoints included general outcome parameters, as well as pharmacokinetics.

Results
Enrolled patients (158 male and 22 female) had a median [IQR] age of 68 [62-74] years. No safety concerns emerged, with 12 SAE's in the EA-230 group and 19 in the placebo group, and no deaths. EA-230 exerted no immunomodulatory effects on IL-6 (median [IQR] AUEC 2730 [1968-3760] for EA-230 vs 2680 [2090-3570] for placebo). GFRiohexol increased post-surgery (mean Δ±SD EA-230: 19±15, placebo: 16±14 mL/min/1.73m2), but was not statistically different between groups (p=0.15). eGFRmdrd increased to a greater extent in the EA-230 group compared to placebo (mean Δ±SD EA-230: 6±11 vs placebo: 2±14 in mL/min/1.73m2, p=0.01). Six patients were classified as having AKI stage Injury in the EA-230 versus 16 in placebo group (p=0.06). 24 Hours after ICU admission, 12% of patients of the EA-230 group were in ICU versus 22% in the control group (p=0.02), and mean and 95% CI in-hospital stay was 195 [171-265] and 234 [192-295] hours in the EA-230 and placebo groups, respectively (p=0.001).

Conclusion
No safety concerns emerged in this first-in-patient study with EA-230. No immunomodulatory effects of EA-230 were observed in cardiac surgery patients. EA-230 appears to exert renoprotective effects. ICU and in hospital length of stay were significantly shorter in the EA-230 group compared to the placebo group.

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Severe Acute Kidney Injury Prediction in the Pediatric Intensive Care Unit (PICU)

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Purpose: Renal Angina Index (RAI) and urinary Neutrophil Gelatinase Associated Lipocalin (NGAL) are predictive of acute kidney injury (AKI) PICU patients (pts). We have integrated the two into an algorithm to enhance prediction of pts at high risk for AKI early in PICU admission.

Methods: All pts admitted to the PICU progress through the algorithm as standard of care. An automated RAI results in the electronic health record (EHR), with a RAI≥8 deemed RAI+. NGAL is collected for RAI+ patients, with NGAL+ defined as ≥150ng/mL. Pts are followed for the primary outcome of the development of KDIGO Stage 2 or 3 AKI (sAKI) based in serum creatinine (SCr) criteria on PICU days 2-4. Other outcomes include >10% fluid overload (FO), initiation of renal replacement therapy (RRT), and PICU and Day 28 mortality. Differences between groups are assessed using Fisher's exact or Mann-Whitney U tests, with p-value <0.05 being considered significant.

Results: 2138 RAIs resulted between 7/1/18 and 3/3/1/19, of which 598 (28%) representing 522 pts had complete data for sAKI analysis on PICU days 2-4. Of these (16.4%) were RAI+. RAI+ pts had higher PRISM III score at admission, 9 vs 3 (p<0.001). The incidence rate of sAKI was higher in RAI+ pts (41.8% vs 3.2%, p<0.001). RRT use was also higher in the RAI+ cohort (12.2% vs 0.6%, p<0.001). Two of the 3 RAI- patients who required RRT did so after exposure to a high number of nephrotoxic medications in the PICU. With the addition of NGAL, sAKI rates continued to be higher in the RAI+NGAL+ cohort compared to RAI+NGAL- and RAI- (59.5% vs 26.9% vs 3.2%, p<0.001) as well as RRT use (24.3% vs 3.9% vs 0.6%, p<0.001). There was no difference between the RAI or RAI/NGAL cohorts in the prevalence or duration of FO. Including all RAIs regardless of SCr availability, the RAI+ population had a longer PICU length of stay (4.5 vs 2.5, p<0.001), higher PICU mortality (13% vs 1%, p=0.001), longer hospital length of stay (10.5 vs 4.7, p<0.001), and higher Day 28 mortality (13% vs 2%, p<0.001).

Conclusion: The use of RAI to screen for the development of sAKI continues to show clinical promise. However, more research is needed into the contribution of nephrotoxic medication exposure after PICU admission to sAKI development in the RAI- and RAI+NGAL- populations, and whether RAI should be adjusted to account for this exposure.

	RAI	RAI and NGAL
Negative Predictive Value	96.8 (95.2, 97.9)	95.6 (94.3, 96.7)
Positive Predictive Value	41.8 (34.9, 49.1)	59.5 (45.1, 72.4)
Specificity	89.5 (86.6, 91.9)	97.1 (95.3, 98.4)
Sensitivity	71.9 (58.5, 83.0)	48.9 (33.7, 64.2)

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Sub-chronic Exposure to Fine Particulate Matter Results in Kidney Injury and Hypoperfusion.

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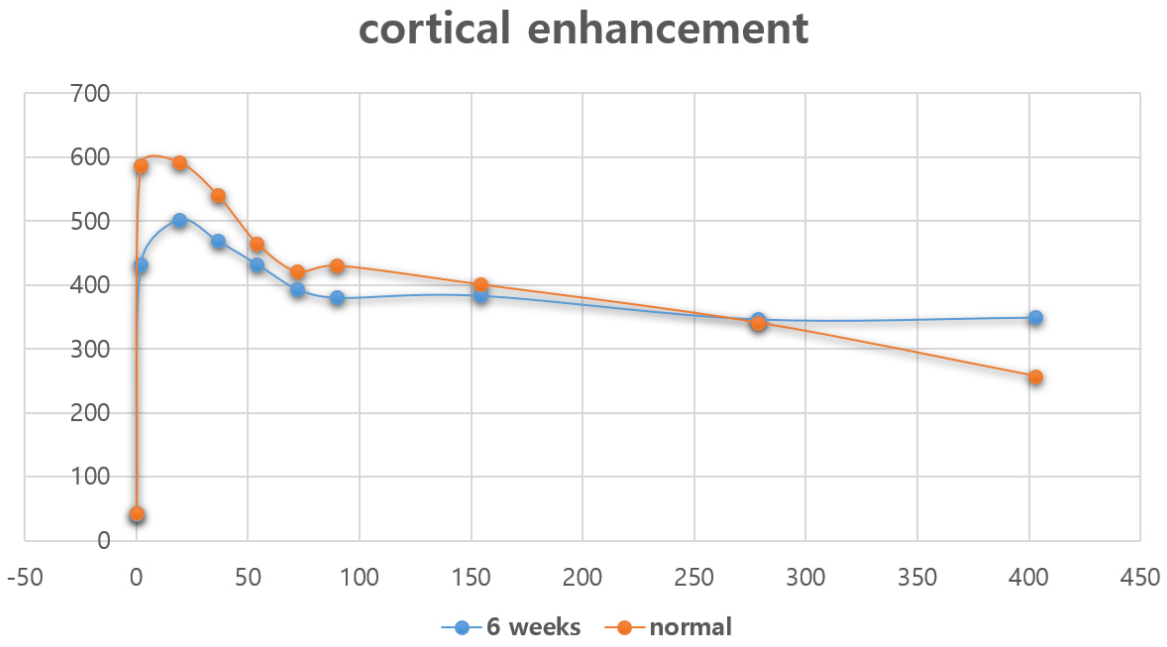
Recent epidemiologic studies have shown significant association between exposure to fine particulate matter and chronic kidney disease incidence and progression to end stage renal disease. In our study, we examined the effect of sub-chronic exposure to inhaled fine particulate matter(PM) on renal injury in experimental rat model. 10 week old Sprague Dawley rats were exposed to Carbon Black particles for 5 hours a day for 3 weeks in an exposure chamber within the fume hood with HEPA-filter. Carbon black concentration measured by Aerosol Mass Monitor was average 248.0±39.4 for PM 2.5 and 384.3±72.0 for PM 4. 1st week Weight loss was apparent in rats exposed to carbon black. Systemic inflammation was significantly increased in PM exposure group. In the kidney, gene expressions of Nox4 and MCP-1 were increased compared to normal control. PM exposed group showed increased tubulointerstitial injury compared to normal group. Renal perfusion was accessed by spectral computed tomography. As expected, direct inhalation of carbon black resulted in lung injury. Prolonged exposure to PM in 36 week old SD rats showed significant increase in inflammation and fibrosis, with prominent tubular injury in the kidney. Contrast enhanced images showed that renal perfusion was decreased and excretion was impaired in the exposure group (Figure 1). Air pollution by particulate matter may be an independent risk for acute and chronic kidney injury.



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Sodium Zirconium Cyclosilicate (SZC) Improves Potassium Balance in Hyperkalemic Hemodialysis Patients: Results from the Phase 3b, Randomized, Placebo-Controlled DIALIZE Study

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Background: Patients with end-stage renal disease frequently have predialysis hyperkalemia (HK) despite hemodialysis (HD). A high serum potassium (sK+) to dialysate K+ (dK+) gradient at the start of HD permits rapid lowering of sK+ but can also be associated with a greater risk of adverse events, such as cardiac arrhythmias and hospitalizations. The phase 3b, randomized, double-blind, placebo (PBO)-controlled DIALIZE trial (NCT03303521) investigated the effect of SZC on predialysis sK+ after the long interdialytic interval in HD patients with HK. To further examine the effect of SZC on potassium (K+) balance, several post hoc analyses were conducted.

Methods: In DIALIZE, 196 patients of mean age 58.1 [SD 13.7] years were randomized 1:1 to receive PBO (n=99) or SZC (n=97) 5 g once daily starting dose on non-dialysis days for 8 weeks, comprising a 4-week SZC dose-titration phase (max 15 g) to achieve target predialysis sK+ 4.0–5.0 mmol/L, and 4-week stable dose evaluation phase (SZC 0, 5, 10 or 15 g). Post hoc analyses included assessment of the number of visits at which patients had sK+ of 4–5 mmol/L and 3.5–5.5 mmol/L, and the maximum sK+ during the evaluation phase. Change in K+ gradient (difference between the predialysis sK+ and dK+) from baseline to end of evaluation phase was also assessed by cross tabulation of categorized dK+ (dK+ 2–3, 3–4, 4–5 and ≥5 mmol/L).

Results: SZC was associated with more patients achieving sK+ 4.0–5.0 mmol/L and being maintained at sK+ 3.5–5.5 mmol/L vs PBO for 1, 2, 3 and 4 visits. 56 patients had severe predialysis HK (sK+ ≥6 mmol/L) in the PBO group during the evaluation period, compared with only 14 in the SZC group. A shift in K+ gradient towards values below the reported higher risk threshold of 3 mmol/L was observed in the SZC group, with 30.6% of patients (n=11/36) moving from gradient 4–5 to 2–3 mmol/L and 55.6% (n=25/45) from 3–4 to 2–3 mmol/L.

Conclusion: These findings suggest that treatment with SZC improves management and reduces the frequency of severe HK in HD patients, which could potentially modify the risks associated with these factors.

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Elevated Urine NGAL Values are Associated with Post-operative AKI in Neonates

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Background
Acute kidney injury (AKI) is common in the NICU and is associated with increased morbidity and mortality including chronic kidney disease. Current diagnosis is suboptimal secondary to unreliability of urine output (UOP) and/or serum creatinine (sCr). Urine biomarkers offer cost-effective predictive promise. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) and its association with AKI is well understood in pediatric cohorts, but the utility in neonates is uncertain.
Methods
Infants admitted to the NICU and undergoing a general surgical procedure were enrolled in this prospective observational study. AKI was defined by the modified neonatal Kidney Diseases: Improving Global Outcomes (KDIGO) definition. uNGAL was measured pre-operatively and at 12, 24, 36, 48, 72 and 96 hours post-operatively using The uNGAL Test™ (BioPorto, Denmark).
Results
A total of 88 neonates underwent 113 surgical procedures (mean corrected gestational age 40 ± 7 weeks) were enrolled. There was a 33% incidence of AKI with average time of diagnosis 24-48 hours. Pre-operative uNGAL levels were not statistically different between no AKI and AKI groups. However, uNGAL values were elevated at all post-operative time points in the AKI compared to those without AKI (Table 1, Figure 1). Development of post-operative AKI directly correlated with peak uNGAL values (417ng/mL vs. 102 ng/mL, p value <0.0001) and preceded clinically apparent AKI (12-24 hours).
Conclusions
Post-operative uNGAL values are elevated in neonates with AKI. Peak uNGAL values occur prior to clinically apparent AKI and could be utilized as an earlier biomarker to detect renal insult. This allows for earlier modifications of treatment plans and avoidance of nephrotoxic medications in post-operative cohorts. While pre-operative urinary NGAL levels failed to identify AKI, we intend to explore the relationship between the relative increase in post-operative uNGAL from baseline as a predictor of AKI and AKI severity.

	Pre-op uNGAL	12 hour uNGAL	24 hour uNGAL	36 hour uNGAL	48 hour uNGAL	72 hour uNGAL	96 hour uNGAL
All	(n=74)	(n=105)	(n=103)	(n=88)	(n=65)	(n=97)	(n=86)
No AKI (n=76)	34[14-103]	29[12-102]	38[14-129]	34[17-101]	37[14-148]	38[16-96]	41[10-111]
AKI (n=37)	55[11-315]	206[27-1280]	199[66-384]	190[38-573]	131[42-463]	211[34-770]	65[24-371]
p value	0.24	0.0033	<0.0001	0.0009	0.0008	0.0039	0.0218

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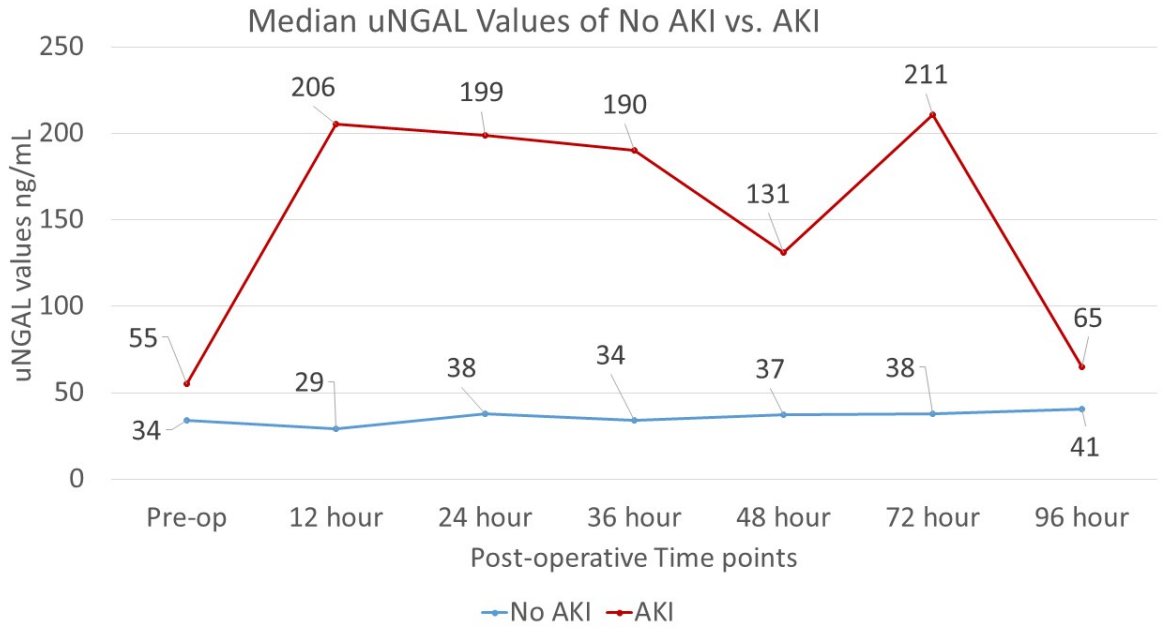

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RBT-1: Therapeutic Renal Preconditioning for AKI Prevention

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Purpose of the Study:
RBT-1 is a novel therapeutic designed to induce oxidant renal preconditioning and prevent acute kidney injury (AKI) induced by multiple injurious pathways. This study was designed to assess the efficacy of RBT-1 in various animal models of AKI: glycerol-induced (rhabdomyolysis), maleate (ATP depletion), ischemia/reperfusion (I/R), and post-AKI progression to CKD (long-term progression). The mechanism of action of RBT-1 was also assessed.

Methods Used:
Male CD-1 mice were pretreated with control or RBT-1 for 18 hours before exposure to one of the following AKI models: maleate, glycerol, or bilateral kidney I/R injury. Vehicle mice served as controls. Mice were sacrificed 18 hours later, and the severity of AKI was determined by blood urea nitrogen (BUN), plasma creatinine (PCr), and renal histology. Mediators of cytoprotection were measured in the kidney prior to AKI induction. Plasma troponin I was measured as a marker of myocardial injury post-AKI induction in the maleate and I/R models. Post-AKI progression to CKD was also assessed in another cohort of mice 3 weeks post-I/R. Finally, the ability of RBT-1 to mitigate ischemic AKI in Nrf2-/- mice was assessed.

Summary of the Results:
RBT-1 was shown to significantly inhibit AKI-mediated increases in BUN and PCr levels in all models tested and to preserve renal histology. It also mitigated AKI progression to CKD. Additionally, RBT-1 resulted in a >90% reduction in AKI-associated troponin I elevations. RBT-1's protective action was mechanistically linked

to activation of the Nrf2 antioxidant/anti-inflammatory pathway, resulting in the upregulation of diverse cytoprotective genes. Further, Nrf2-/- mice were resistant to RBT-1-mediated protection against AKI.

Conclusions:
RBT-1 represents a novel therapeutic approach for the prevention of AKI. Treatment with RBT-1 demonstrates kidney protection in various animal models of AKI, including post-AKI progression to CKD. RBT-1 mediates kidney protection by upregulating markers of the major antioxidant transcription factor Nrf2. These data highlight the broad range of activity of RBT-1. A Phase 1 study of RBT-1 is underway and will be completed in early 2020.

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Predicting Acute Kidney Injury After Cardiac Surgery

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Background: Acute kidney injury (AKI) is a common and important complication after cardiac surgery. It is associated with increased risks of mortality, adverse outcomes and higher medical expenditure.
Objectives: This study aimed to develop and validate a risk prediction model for AKI after cardiac surgery.
Methods: A total of 1,063 patients with complete data admitted for cardiac surgery between 2009 and 2015 in a tertiary referral hospital were included.
Results: The multivariable logistic regression analysis showed that body mass index, aortic or valve surgeries, hypertension, emergent surgery, preoperative hemoglobin, post-operative APACHE3 and SOFA scores were predictor factors of AKI with a modest area under the curve (AUC) of 77.4% (95% confidence interval [CI]: 74.2% to 80.6%). By adding age, diabetes mellitus, atrial fibrillation, pre-operation creatinine into the prediction model for AKI stage 3, the model performance of discrimination was satisfied with an AUC of 84.7% (80.9% to 88.6%).
Conclusions: By using the clinical prognostic system with computer assisted data collecting system, the score might be useful in clinical usage.

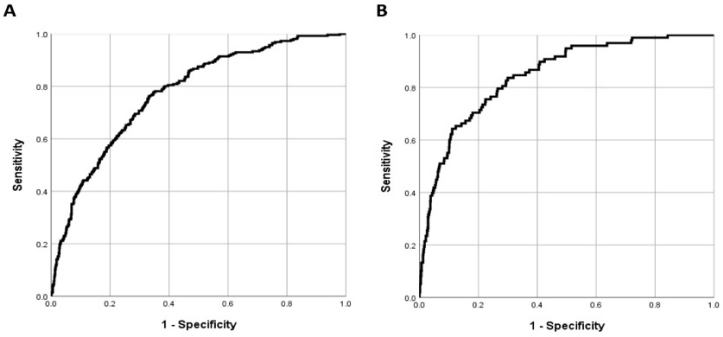

Figure 1. The receiver operating characteristic curve analysis of the proposed model on predicting acute kidney injury (KDIGO class ≥1) (**A**) and KDIGO class ≥3 (**B**). The area under the curve was 77.4% with a confidence interval of 74.2% to 80.6% for KDIGO class ≥1; the area under the curve was 84.7% with a confidence interval of 80.9% to 88.6% for KDIGO class ≥3.

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High dose thiamine for dialysis requiring acute kidney injury in patients with sepsis: a nationwide inpatient database study in Japan

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Background:
Some studies have recently reported that high dose thiamine may reduce mortality and progression of acute kidney injury (AKI). However, the sample sizes of these studies are small and the significance of thiamine is still controversial. Therefore, we aimed to investigate the association of thiamine with in-hospital mortality and short-term non-recovery from renal replacement therapy (RRT).

Methods:
We conducted a retrospective observational study using the nationwide Diagnosis Procedure Combination inpatient database during a period between April 2010 and March 2017. We identified patients with septic AKI who required continuous RRT within 2 days of admission.
Patients were divided into those who received high dose (100 mg or more) thiamine within 2 days of admission (thiamine group) and those who did not (control group). We performed propensity-score inverse probability of treatment weighting (IPTW) to adjust for measured confounders. Primary outcome was 28-day mortality and secondary outcome included in-hospital mortality and a composite outcome of death and RRT-dependence at discharge.

Results:
We identified 9,927 patients eligible (2809 in thiamine group and 7118 in control group). The 28-day mortality was 31.5% (884/2809) in thiamine group and 30.5% (2168/7118) in control group. After adjustment for confounders (a total of 49 covariates, including comorbidities and treatments) by IPTW, there were no significant differences in 28-day mortality between the two groups (adjusted risk difference, 0.2%; 95% adjusted confidence interval [CI], -2.0% to 2.3%). There were no significant differences in in-hospital mortality (0%; -2.4% to 2.3%), in composite-outcome (-0.4%; -2.8% to 2.0%), nor in RRT dependence at discharge (-0.4%; -1.5% to 0.7%).

Conclusions:
High dose thiamine was not associated with decrease in mortality or RRT-dependence at discharge in patients with septic dialysis-requiring AKI.

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Proenkephalin, a Novel Biomarker for Kidney Function, is Earlier in Detecting Acute Kidney Injury Compared to Creatinine.

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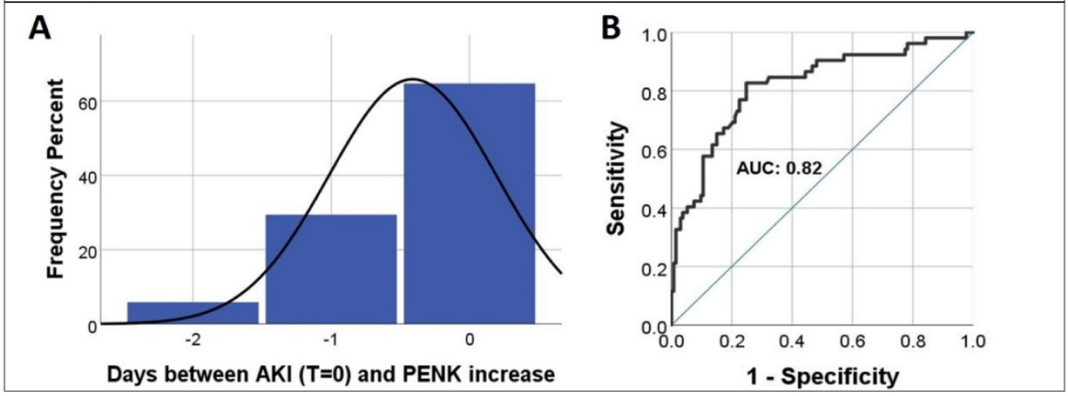
Background Acute kidney injury (AKI) in critically ill patients is independently associated with prolonged hospital stay and impaired clinical outcomes. In daily clinical practice, creatinine is the most frequently used biomarker to assess kidney function. However, plasma creatinine is a notoriously insensitive and late marker, consequently hampering the timely diagnosis of AKI and research related to novel therapies for AKI. The novel plasma biomarker proenkephalin (PENK), a byproduct of enkephalins, is currently studied for its reflection of kidney function. Kinetics of PENK during a period of AKI compared to creatinine are unknown. This study aims to determine whether or not the plasma biomarker PENK is able to diagnose AKI earlier than plasma creatinine.
Methods In this prospective study, all patients admitted to our Intensive Care Unit (ICU) with an anticipated ICU length of stay >1 day and not already fulfilling AKI criteria on admission were included. Plasma creatinine concentrations were determined using daily routine sampling. Residual material was collected to determine PENK concentrations. AKI was diagnosed using the KDIGO criteria: creatinine concentration rise of 26.5 µmol/L within 2 days (stage 1). One sample t-test was used to assess the difference in time of the increase before and decrease after the occurrence of AKI. Receiver operating characteristics (ROC) curves were created to assess the diagnostic performance of PENK.
Results We included 189 ICU patients, median [IQR] age was 65 [55-72] years and 119 patients (63%) were male. 56 patients (24%) developed AKI during ICU admission. PENK concentrations increased (mean±SEM) 0.4±0.08 day earlier than creatinine ($p<0.0001$), figure 1-A. When AKI resolved and creatinine decreased, PENK concentrations decreased 0.7±0.22 day earlier. The area under the ROC curve of the PENK concentration the day before AKI diagnosis was 0.82 (95%CI 0.75-0.89), with an optimal cut-off value of 66 pmol/L resulting in sensitivity and specificity of 83% and 75%, respectively, see figure 1-B. The positive and negative likelihood ratio was 3.3 and 0.30, respectively.
Conclusion PENK is freely filtrated through the glomerulus without active secretion or resorption and may therefore be capable to detect AKI more swiftly compared to creatinine. Furthermore, PENK plasma concentrations the day before diagnosis of AKI as a diagnostic test is classified as good in an unselected population of critically ill patients.

Figure 1. A) Days between AKI diagnosis and PENK increase B) ROC curve of PENK at 1 day before AKI diagnosis



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Discovering Risk Factors Associated with Inpatient Acute Kidney Injury across Age Groups

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Objective: Acute kidney injury (AKI) is a challenging medical problem and is associated strongly with age. However, risk factors for AKI in the general inpatient population across age groups has not been evaluated systematically. We built a machine learning model to identify clinical factors predictive of AKI in inpatients across age strata.

Methods: We extracted a retrospective cohort of adult patient encounters from all inpatient units of a tertiary hospital from 2008 to 2016 and stratified it into four age groups: 18-35, 36-55, 56-65, and >65. We collected 1,888 clinical factors for each encounter including demographics, medications, labs, vital signs, and past and admission diagnoses. AKI was defined using the KDIGO serum creatinine criteria. We applied the gradient boosting machine (GBM) for AKI prediction and proposed variations of the shapely additive explanations (SHAP) method to measure importance of factors. The model was trained and validated through 10-fold cross-validation. The model was evaluated in terms of area under the receiver operating curve (AUROC), stability of important factors ranked by SHAP, and consistency to expert knowledge.

Results: Among 76,957 eligible encounters, 7,259 (9.43%) encounters had AKI and 38,887 (50.53%) had patients with age > 56. AUROC achieved for the four age groups were 0.85 [95% CI: 0.80-0.88], 0.86 [95% CI: 0.83-0.89], 0.87 [95% CI: 0.86-0.90], and 0.87 [95% CI: 0.86-0.90], respectively. The proposed weighted average SHAP value showed the highest stability for ranking predictive factors. Compared to expert knowledge, absolute consistency rates of the top 150 ranked factors for each group were 78.4%, 77.2%, 81.3%, and 79.5%, respectively. We observed the risk of many factors varied across age groups; for example, low BMI was found to be associated with higher AKI risk in younger patients, but high BMI was found to be associated with higher AKI risk in elderly patients. Some medications showed high predictive risk for AKI only in certain age group; for example, aztreonam in younger patients and deslanoside in older patients, which may be due to age distribution differences underlying the diseases being treated with the medication.

Conclusion: We identified a set of important risk factors of AKI for four age groups and observed heterogeneity in the factors across groups, demonstrating age-specific risk differences. The results will inform decision support systems to enhance personalized AKI prevention.

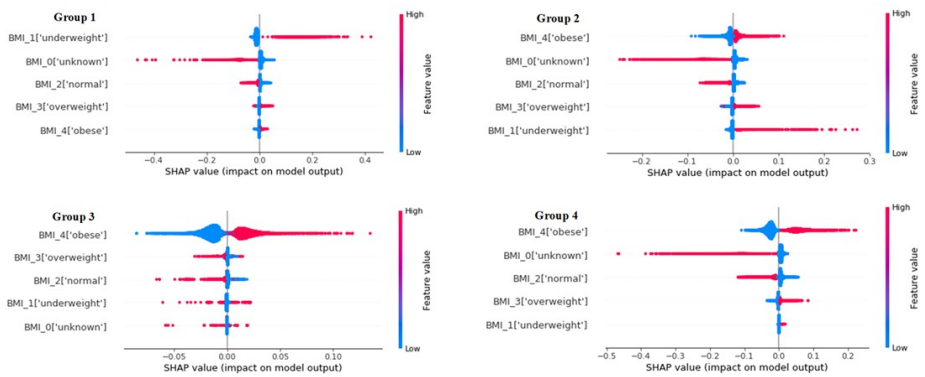

Figure. Weighted average SHAP value plot for BMI. The higher the SHAP value of a clinical factor, the higher risk of AKI due to that factor. Each dot in the plot is a person with that factor value. Dots are colored by the factor value for that person and piled up vertically to show density.

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AKI-Sapere: A Novel Blood Test that Predicts Cardiac Surgery-Associated Acute Kidney Injury

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[1]*Sapere Bio,* [2]*Baylor Scott and White,* [3]*Johns Hopkins,* [4]*WakeMed Health*

Hospital-acquired AKI is a devastating adverse event associated with significant morbidity, mortality, and healthcare costs in both the short- and long-term. Efforts to prevent AKI have peaked with the optimization of procedure-based risk. However, high incidence persists because patient-based risk remains difficult to assess clinically. We postulated that measures of "molecular age" could identify patients at-risk of AKI before cardiac surgery, opening the window of opportunity for intervention. We developed AKI-Sapere, a risk prediction model where 96% of prediction is driven by a biomarker of aging, CDKN2A. In a developmental cohort of 96 patients, pre-operative measurement of AKI-Sapere identified 83% of patients who subsequently developed AKI after cardiac surgery (91% NPV).

We are currently conducting a prospective, multi-center validation study of AKI-Sapere in 572 cardiac surgery patients. The primary outcome is prediction of any stage of KDIGO-defined AKI. Secondary outcomes include prediction of stage 2/3 AKI as well as prediction of longer-term AKI-related adverse events (at 30 days) including persistent kidney impairment, major adverse cardiac events (MACE), and/or major adverse kidney events (MAKE). Inclusion criteria are broad with the aim of generating real-world evidence.

To power AKI intervention trials, investigators have historically combined chronological age and co-morbidities to enrich for AKI. Consequences included low enrollment, costly trials, compromised patients with extensive co-morbidities, and ultimately, failure of many promising therapeutics. Because AKI-Sapere can identify patient-based risk, it can be used to enroll patients at known risk for AKI, dramatically reducing the number sites and costs associated with AKI trials. Additionally, investigators can expect to enroll healthier and potentially more treatable patients (ie, patients with fewer and/or less severe co-morbidities) compared with historical cohorts. Thus, AKI-Sapere can be a high-impact clinical tool to both improve individual patient care and accelerate evidence development for AKI interventions.

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Blood Urea Nitrogen/Creatinine Ratio Less To Twelve Predicts Acute Tubulointerstitial Nephritis In Acute Kidney Injury

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INTRODUCTION: Acute tubulointerstitial nephritis (ATIN) is a lesion that confines a deleterious effect on renal function based on an inflammatory infiltrate in the renal interstitium. In acute kidney injury setting, the incidence of ATIN is reported in about 13%-27% according to different series. To date, no biomarker allows us to make an early diagnosis of ATIN

Purpose of the study: To assess if the BUN/creatinine ratio of less than 12 correlates with the histopathologic findings of ATIN in the context of the acute kidney injury.
METHODS: Cohort, prospective, clinical, pilot trial. Patients with acute kidney injury (AKI) who went under renal percutaneous biopsy (RPB) guided by ultrasound histopathologic analysis was performed. Patients with AKI due to obstruction or prerenal etiology were excluded. Results from 42 patients with a BUN/creatinine ratio of less and higher than twelve and histopathologic results of ATIN were analyzed.
RESULTS: In one year, there were made a total of 42 RPB, with a median age distribution of 44.8 years (19.4 SD). Males were the most biopsied sex (51.5%). There was an inverse correlation between the BUN/creatinine ratio and the histopathologic result of ATIN (rho= -0.4, p=0.022) meaning that the smaller the ratio greater the possibility of ATIN. The ROC curve indicated the cutoff of 12 in the BUN/creatinine ratio had the best performance in the diagnosis of ATIN, with AUC of 0.73 p=0.04. There were found a significant association between patients with BUN/creatinine ratio less than 12 and the histopathologic findings of acute tubulointerstitial nephritis with a sensitivity of 76% and specificity of 81% PPV of 81.2% and NPV of 76.4% Odds ratio 14.1 CI 95%: 2.6-75.7, p = 0.0021. In the multivariate regression analysis, it was found that the BUN/ creatinine ratio was the only factor statistically significant.
CONCLUSION: We demonstrate that there is correlation between the BUN/creatinine ratio of less than 12 in the acute kidney injury with histopathologic findings of ATIN with an odds ratio of 14.1. This finding will allow us to implement more effective preventive and therapeutic strategies with this pathology.

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The predictive ability of urinary biomarkers for progression of Acute Kidney Injury in critical illness.

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Introduction and Aims: Acute Kidney Injury (AKI) is a common hospital complication associated with high morbidity, mortality and the risk of progression to CKD. AKI progression biomarkers are needed to inform clinical management and the design of future clinical trials. The Dublin Acute Biomarker Group Evaluation (DAMAGE) Study is a prospective multi-center observational study with a heterogenous cohort of critically ill patients. We hypothesised that urinary NGAL, Albumin, Cystatin-C, KIM-1 and LFABP-1 would predict clinical progression to stage III or death in 7 days or RRT or death in 30 days.
Methods: The biomarker day of diagnosis values of urinary NGAL, Albumin, Cystatin-C, KIM-1 and LFABP-1 were measured. There then compared using logistic regression modelling and cross-validation with the clinical model alone for the prediction of the primary outcomes of stage III or death in 7 days or RRT or death in 30 days. The clinical model was composed of serum creatinine and urine output (ml/hr).
Results: 143 patients had an AKI in the first seven days of their ICU stay, of whom 47 progressed to a higher Stage/ RRT/ Death in 30 days. 105 patients had a Stage I/II AKI within 48 hours of admission. Of this group, 20 (19%) progressed to Stage 3/ Death within 7 days.
Urinary Albumin had a ROC AUC of 0.78 (95% CI 0.77-0.78), NGAL 0.7 (95% CI 0.69-0.71) and LFABP-1 0.76 (95% CI 0.75-0.77) for the prediction of progression of early AKI in 7 days. The addition of Albumin to the clinical model resulted in a ROC AUC of 0.76 (95% CI 0.75-0.78) compared with 0.66 (95% CI 0.65- 0.67) for the clinical model alone (P<0.001).
Conclusions: In this study of AKI progression, urinary Albumin was the strongest single predictor for the progression of AKI in 7 days. The addition of Albumin improved the prediction of KDIGO Stage 3 or death in 7 days over a clinical model of serum creatinine and urine output.

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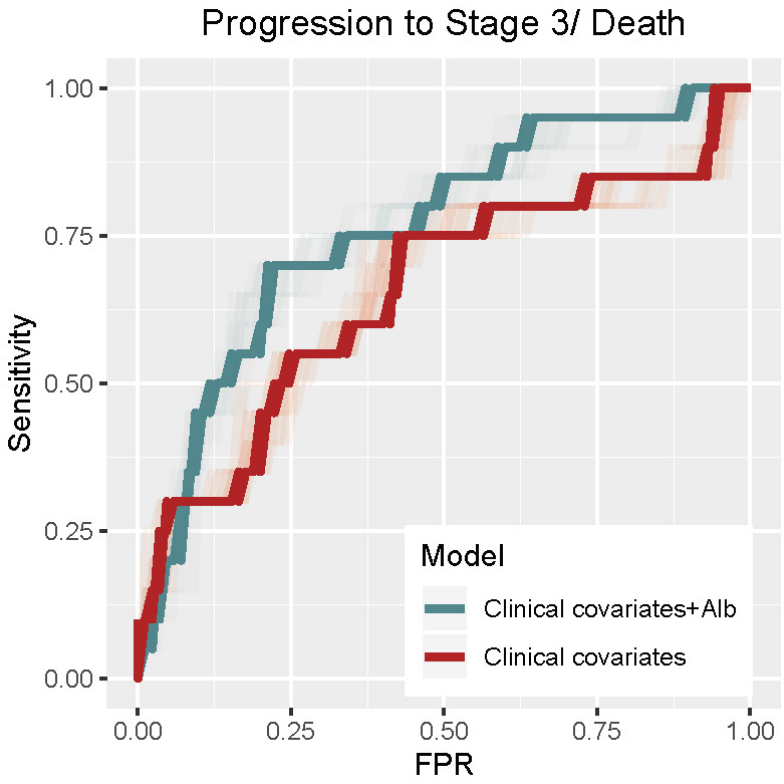

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Postoperative Behavior of Renal Functional Reserve in Patients Undergoing Cardiac Surgery

Félix A Matías[1], Armando Vázquez[1], Magdalena Madero[1], Francisco M Baranda[1], Rolando J Álvarez[1], Maria Perez[1], Edilia Tapia[1], Laura G Sanchez[1], Eneida Bailon[1], Ricardo S Guerrero[1]

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• Purpose of the study

The Renal Functional Reserve (RFR) correspond to the ability to increase Glomerular Filtration Rate (GFR) after a physiologic or pathologic stimulus. Recent publications have addressed the relation between baseline RFR and postoperative acute kidney injury (AKI). To our knowledge, the immediate postoperative behavior of RFR has not been described. As secondary aims we evaluated potential biochemical surrogates for RFR.

•Methods used

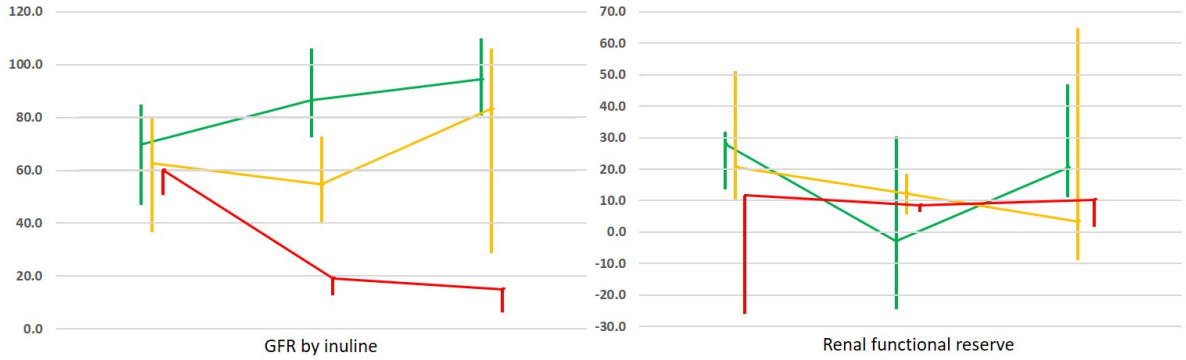
This is a prospective cohort study, approved by the local ethic and research committee in the Instituto Nacional de Cardiologia Ignacio Chavez in Mexico City. Adult patients with GFR between 30 and 90 ml/min who underwent elective cardiac valve surgery were included. GFR was assessed with inuline clearance as the gold standard, and it was evaluated before and after an intravenous infusion of amino acids and dopamine for renal reserve stimulus. RFR was calculated on day -1, +1 and +3 of cardiac surgery. Short creatinine clearances, creatinine excretion and estimated GFR by cystatin C before and after the stimulus were evaluated as potential surrogates.

• Summary of the results

Eighteen patients were included, 7 (38.9%) developed AKI and only 2 of them had severe and persistent AKI. Preoperative GFR by inuline was 68.6 (46.8-78.4) ml/min/1.73m2, which increased to 75.0 (52.6-93.5) on day +1 and 89.2 (48.0-103.7) on day +3. Baseline RFR was 27.4 (10.7-43.9) ml/min, which decreased to 10.5 (-9.1-20.9) on day +1 and 18.5 (1.0-29.1) on day +3. In patients with no AKI, GFR is increased by using its RFR (green line). With transient AKI, a smaller reduction in RFR lead to no increment in postoperative GFR on day +1 (orange line). In patients with severe persistent AKI, a lower baseline RFR available showed a significant drop in GFR (red line).
Rho coefficients in comparison to RFR by inuline were: 0.210 (p=0.131) for serum creatinine, 0.309 (p=0.024) for cystatin C, 0.574 (p<0.001) for short creatinine clearance, and 0.525 (p<0.001) for short creatinine excretion.

• Conclusions

Postoperative behavior suggests the use of RFR as a mechanism of compensation (kidney adaptation) in patients who do not develop clinical AKI, such incapacity could explain the development of postoperative AKI. Short creatinine excretion measurement should be evaluated as a potential surrogate for changes in GFR including the estimation of RFR.



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Using Propensity Score Methods to Determine the Incidence of Major Adverse Kidney Events in Pediatric Patients admitted to the Intensive Care Unit

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Introduction: There is increasing evidence that Acute Kidney Injury (AKI) is associated with adverse outcomes in critically ill pediatric patients. However, most data are from multivariate regression analyses of retrospective databases. Even well-constructed regression models may be unable to answer questions about association vs. causation and confounding vs. true effect. Our aim was to use propensity score matching to study pediatric AKI and outcomes.
Methods: We evaluated 11,565 intensive care unit (ICU) admissions from 7/1/2009 to 12/31/2018 at Seattle Children's Hospital. We excluded all readmissions, patients aged <6months or >18years, ICU admission <48hrs, and encounters with missing variables. In total, 582 patients were included in analysis. Our primary

outcome measure was Major Adverse Kidney Events at 30 days (MAKE30): creatinine >200% of baseline, eGFR <60mL/min/1.732, dialysis dependence, or mortality before 30 days. Daily propensity scores for the development of AKI were generated. On the day a participant developed AKI, they were matched to a non-AKI control with a similar propensity score on that day using 1:1, nearest neighbor matching. Logistic regression was used to test association between AKI status and MAKE30 in propensity matched cohorts.
Results: 155 patients were included in the propensity matched cohort. In the unmatched cohort, participants with AKI had higher PRISM III scores (9.9 vs. 5) as well has lower baseline platelets (131 vs 203, [thousands of platelets]) compared to those without AKI. In the matched cohort, the imbalance between PRISM III scores (12.3 vs. 9) and platelet count (120 vs. 125) decreased between participants with and without AKI. Age, weight, an history of bone marrow transplantation was similar regardless of AKI status in both the unmatched and matched cohorts. AKI associated with the MAKE30 outcome in the unmatched (Odds Ratio [OR]: 29.6; 95% CI: 2.04-427; p=0.013) and propensity score matched cohort (OR: 23.3; 95%CI: 3.06-177; p=0.0025).
Conclusion: Propensity score matching reduced covariable imbalance between participants with or without AKI during the first seven days of admission to the pediatric ICU. Using a propensity score matched cohort, AKI status strongly associated with the development of major adverse kidney events at 30 days following ICU admission. Further investigation and refinement of this analysis is ongoing.

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Severe Leptospirosis with Multiple Organ Failure Treated with Renal Replacement Therapy, ECMO and Hemoperfusion using HA 330: A Case Series

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[1]*National Kidney and Transplant Institute*

Background: Leptospirosis is an endemic zoonosis in the Philippines precipitated by disasters and extreme weather events. It emerged as an important cause of pulmonary hemorrhage and acute kidney injury. This case series aimed to describe the use of hemoperfusion therapy using HA 330 cartridge in patients with severe leptospirosis who were on extracorporeal membrane oxygenation (ECMO) together with renal replacement therapy (RRT).

Methods: We included patients with severe leptospirosis who acute respiratory distress syndrome and acute renal failure. All patients received a minimum of 3 hemoperfusion treatments using HA 330 cartridge for 3 hours for 3 days and underwent additional treatments depending on their hemodynamic status. Blood flow rates were kept between 150- 200mL/minute. Sequential organ failure assessment (SOFA) score, demand for inotropes to achieve a MAP 65 (µg/h*mmHg-1), HsCRP and Procalcitonin were collected at the baseline until after the last hemoperfusion therapy. Renal and patient survival were also noted.

Results: There were 19 patients who were included in this case series. The SOFA score decreased by 16- 44% after the third hemoperfusion. A decrease of HsCRP 12- 90% and decrease of procalcitonin of 52- 99%. Norepinephrine was tapered to off after third hemoperfusion. Fourteen patients survived and recovered their pulmonary and renal function. Five patients died.

Conclusion: There was a decrease of Procalcitonin, HsCRP levels, SOFA scores, and decrease of inotropes after the first hemoperfusion, allowing adequate blood pressure support to do the ECMO and renal replacement therapy. It stabilized the hemodynamic status of the patient.

RRT TECHNIQUE CHARACTERISTICS

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Metabolic effects of citrate- calcium-gluconate use for continuous veno-venous hemodialysis

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Purpose of the study: The use of calcium chloride during SRRT is recommended by protocol. However, since calcium chloride is not available in our country, calcium gluconate is used. We aimed to demonstrate the effect of different blood flow rates (150ml / min and 130ml / min) on acid-base and electrolyte balance in continuous venovenous hemodialysis using citrate-calcium gluconate in our study and to determine the use of calcium gluconate in appropriate blood flow rate.
Material and Method: In our study involving 113 patients who underwent hemodialysis between 01 January 2014 and 30 September 2017 at the Department of Anesthesiology and Reanimation Intensive Care Unit, 13 patients were excluded because the duration of dialysis was less than 24 hours . A total of 100 patients with complete remission were studied retrospectively. The patients are divided in two groups according to blood flow rate, 150ml/min and 130ml/min respectively . Their ionized calcium levels, sodium, potassium, bicarbonate levels, pH values, lactate levels in the prefilter and postfilter blood gas analyzes taken every 6 hours are recorded from patient files and compared with statistical methods.
Results: In both groups, it was found that most of the initial acidosis recovered after 48 hours. The increase in pH value was significant after 30 hours in the group with 130 ml/min blood flow rate and after 18 hours in the group with 150 ml/min blood flow rate, suggesting that high blood flow rate is more effective at increasing pH. No new acidosis or alkalosis developed in both groups. There was no significant difference between the two groups in terms of the effect of blood flow rates on electrolyte balance ($p<0.05$). Lactate levels decreased in both groups, we think that decline was the result of the improvement in clinical conditions of patients rather than the clearence effect of renal replacement.
Conclusion: During calcium gluconate use instead of calcium chloride in continuous venovenous hemodialysis with citrate anticoagulation, metabolic status should be closely monitored and blood flow rate should be adjusted according to acid-base balance.

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Single Center Case Study on Acute Dialysis with a Dialysate Flow Rate of 300mL/min compared to ≥ 500mL/min

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[1]*Outset Medical,* [2]*St. Francis Medical Center, Lynwood CA*

Background: Conventional hemodialysis is usually prescribed at a dialysate flow rate (Qd) of 500 mL/min or greater. Tablo® is an easy to use hemodialysis system with on demand dialysate production, two way wireless capability, and reduced water usage with a Qd of 300mL/min designed to facilitate innovation of dialysis care in all settings. Previously published modeling and real world data have demonstrated that patients can achieve adequate urea clearance with Tablo in the acute and chronic settings.

Purpose: To report on the clinical experience in an acute hospital setting of consecutive patients treated with the Tablo® Hemodialysis System at Qd 300 mL/min and a conventional system at Qd 500mL/min or greater during their hospitalization.

Methods: Retrospective review of patients admitted to St Francis Hospital who, during their acute hospitalization, received dialysis treatments on both Tablo and a conventional dialysis device. Treatment data including dialysis prescription, treatment time and dialyzer were recorded. To mimic the current standard of acute care, clinical lab results of blood urea nitrogen (BUN) and potassium (K) were obtained on the day of therapy and the day following therapy. Timing of dialysis in relation to the timing of the two lab results was not recorded.

Results: Over 13 months, 105 of 289 patients dialyzed on Tablo also treated on an FMC T machine during their hospitalization. Average treatment time on both devices was 3.3 hours/treatment. Treatments were primarily performed on Revaclear 300 dialyzers with larger dialyzers (Revaclear 400 or F180) used in 25% of Tablo treatments and 28% of FMC treatments. Table 1 (n= treatments) shows the average day of and day after results by device.

Discussion:
As can be seen in the acute setting, the average treatment time was less than four hours. With equivalent treatment times and dialyzers, day after treatment results for both potassium and BUN on Tablo at Qd 300mL/min compared to a conventional device at Qd 500mL/min or greater were similar. Selection bias related to patient size and dialysis access type were minimized by allowing patients to serve as their own controls.

Conclusion: In the less predictable acute environment, the Tablo System at Qd 300mL/min reduces water usage associated with dialysis and can yield similar results to conventional systems at Qd 500mL/min or greater.

Parameter	Tablo (n=172)	FMC-T (n=191)
Treatment Time (hrs)	3.3	3.3
K (mEq/L)		
Day of Avg	5.1	5.1
Next Day Avg	4.4	4.2
Pre-K = 5.5	39.0%	33.5%
BUN (mg/dL)		
Day of Avg	75	75
Next Day Avg	52	50

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Hemodialysis catheter suction toward the vessel wall during continuous renal replacement therapy can be prevented using a hand technique

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Background:Sudden dysfunction of vascular-access hemodialysis catheters can cause serious complications associated with continuous renal replacement therapy (CRRT). Suctioning of the catheters' arterial pores toward the blood vessel wall is one of the main catheter-related problems during CRRT. Unfortunately, it cannot be clearly observed during CRRT; thus, assessing its pathophysiological mechanism in vivo is difficult. We applied an ex vivo evaluation system.Purpose:This study aimed to investigate whether a certain hand technique can prevent the catheters from suctioning the vessel wall during CRRT.
Methods: The blood purification machine TR-525 and the blood circuit U-520SZ were used. Two catheters were connected to the blood circuit. Considering CRRT, the catheter blood flow was set to 80 and 120 mL/min. An ex vivo evaluation system using a swine azygos vein was developed for this study. The catheters were inserted into an extracted vein of approximately 10 mm in diameter and 200 mm in length. The vein was connected to the blood circuit and filled with 50% glycerol solution, with a blood flow rate of 300–700 mL/min. The arterial pores of the catheters were then positioned near the vessel wall. As the arterial pores of the catheter attempted to suction the vessel wall, a hand technique was performed, in which is the catheters were moved in a pullout direction or rotated to the right direction, to prevent the catheters from suctioning the vessel wall.
Results:The suctioning effect of the catheters toward the vessel wall did not improve by moving them in a pullout direction when the vein blood flow was 300 mL/min and the catheter blood flow was 80 and 120 mL/min. Conversely, when the vein blood flow was 700 mL/min and the catheter blood flow remained unchanged, it improved after the catheters were moved in a pullout direction. Meanwhile, the phenomenon also improved after the catheters were rotated at 120° to the right direction when the vein blood flow was either 300 or 700 mL/min and the catheter blood flow was 80 and 120 mL/min. It also improved after the catheters were rotated at 30° to the right direction when the vein blood flow was 700 mL/min (not 300 mL/min) and the catheter blood flow remained to be 80 and 120 mL/min.
Conclusion:The hand technique may help prevent the catheters from suctioning the vessel wall. Furthermore, by rotating the catheters, the arterial pores were moved away from the vessel wall, indicating the technique's effectiveness.

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CVVHF in a patient with sepsis, acute renal injury and severe acute hypernatremia.

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Introduction: Hypernatremia is one of the most common electrolyte complications in the intensive care unit. Its incidence increases with the indiscriminate use of crystalloid solutions in the resuscitation phase, as well as the use of sodium bicarbonate in patients with metabolic acidosis. It is often accompanied by acute renal injury, and together they worsen the patient's survival prognosis.

Objectives: To describe the clinical case of an elderly woman with leukemia, acute renal injury and severe hypernatremia that required CRRT with the need to adjust the concentration of sodium in the replacement solution to avoid serious variations of plasma sodium that could cause serious damage cerebral.

Case report: A 67-year-old woman with a diagnosis of acute myeloid leukemia in treatment with chemotherapy, complicated with urinary and pulmonary sepsis that developed hypernatremia secondary to the intense administration of crystalloid solutions and endovenous sodium bicarbonate. Nephrology assessment was requested for creatinine elevation consistent with acute renal injury KDIGO 3 induced by sepsis, anuria, and serum sodium of 172 mEq / L.
The management of hypernatremia with hypotonic solutions was initiated, however, due to fluid overload greater than 10% and hemodynamic instability, it was decided to initiate renal replacement treatment with CVVHF.
The sodium concentration in the replacement solution for hemofiltration was adjusted, according to the formula referred to by Yessayan et al, to obtain a concentration of 160 mEq / L or 800 mEq in 5 liters of replacement volume, with adjustment according to plasma sodium results; usually with a delta (plasma sodium / sodium in replacement liquid) of 10 mEq. The therapy was prescribed with Qb 250 ml / min, Qr-pre 1400cc, Quf 100 ml / hr, with the aim of correcting plasma sodium at approximately 6 mEq / L in 24 hours.
In 72 hours, the patient adequately tolerated CRRT, with a decrease in plasma sodium to 155 mEq / L, however she presented bleeding, and progression of sepsis, and, unfortunately, she died.

Discussion and Conclusions: The use of CRRT in severe disnatremias, especially in patients with acute kidney injury or fluid overload, has been demonstrated by several authors. Severe hypernatremia is most important complication as acute neurological injury that may be irreversible. Using CVVHF is very useful for very complex cases and can improve the prognosis of the patient.

Day	-4	-3	-2	-1	0	1	2	3
Corrected Sodium (mEq/L)	156	166	185	183	172 (CVVHF)	168	158	155
K (mEq/L)	2	2.4	2.3	2.2	3.7	3.6	3.7	4.2
BUN (mg/dL)	29	35	42	43	69	68	44	24
Creatinine (mg/dL)	1.52	1.44	2.04	2.32	4.97	4.5	3.1	1.68
Glucose (mg/dL)	138	128	228	310	364	234	190	95

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Efficacy and Safety of Calcium-Containing Dialysate under Regional Citrate Anticoagulation in Continuous Renal Replacement Therapy

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Purpose of the study
Regional citrate anticoagulation(RCA) is the preferred anticoagulation method for continuous renal replacement therapy (CRRT), recommended by KDIGO. For the effective chelation of calcium in blood entered into the circuit, calcium-free dialysate is generally used. However, due to the shortage of calcium-free dialysate, the use of RCA for CRRT is getting limited. Our institute used RCA with calcium-containing dialysate in all the patients receiving CRRT from 2016. In this study, we report our experience focused on the efficacy and safety of RCA with calcium-containing dialysate.

Methods
We retrospectively reviewed consecutively collected patient and filter data used in CRRT at UCSD from the January 1st, 2017 to December 31th, 2017. All participants were treated with RCA under calcium-containing dialysate. We checked its efficacy by checking filter performance. We reviewed filter change reasons according to the filter longevity. For safety measurement, the prevalence of metabolic complications was calculated. Membrane function and complications were also evaluated in a subgroup of patients with sepsis or liver disease.

Results
A total of 571 filters from 128 patients were included. Median filter life was 33.0(16.0-69.0) hours. Of the 571 filters, filter change reasons were recorded in the 356 filters. Among them, 129 filters were changed within 24 hours however, 58.9% of the filters were changed due to the events unrelated to the therapy, 8.5% of the filters were changed due to access problem and only 32.5% of the filters were changed for filter clotting or low efficacy. In filters that were changed between the 25 and 48 hours of CRRT, only 35% were changed due to clotting or low efficacy. When we excluded filters without filter changing reasons and filters changed unrelated to the therapy, median filter longevity was 50.0(22.0~118.0) hours.

The most common metabolic complication was systemic hypocalcemia with a prevalence of 77.1% in all applications. However, 87% of all hypocalcemia were mild with the ionized calcium level between 0.95 and 1.10 mmol/L. Systemic hypercalcemia was only 0.1% of all applications. Metabolic acidosis was the 2nd most common complication(48.5% per application) and metabolic alkalosis were observed only in the 1.9% of all application. A calcium gap higher than 2.5 was observed in 9.0% of the application. In all included patients, 24.6% had liver disease and 36.1% had sepsis. Median filter longevity was 26.0 (14.0-51.0) for liver disease and 26.0(15.0~43.3) hours for sepsis that were shorter than the general. In both of the cases, hypocalcemia and hypophosphatemia were the most common metabolic complications. The prevalence of calcium gap higher than 2.5 was 38.3% in liver disease and 18.4% in septic patients. In patients with liver disease, no case of hypercalcemia was observed.

Conclusion
Calcium containing dialysate was safe and effective in the RCA of CRRT. Even in patients with liver disease, RCA was usable with adequate monitoring and intervention for metabolic complications.

RRT APPLICATIONS AND TARGETED INTERVENTION

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Combined Hemodialysis and Hemoperfusion in Successful Treatment of a Patient with Multiple Organ Failure from Severe Acute Pancreatitis

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BACKGROUND
Severe acute pancreatitis (SAP) is defined by 2012 Atlanta Classification for Acute Pancreatitis as pancreatitis with multiple organ failure lasting for more than 48 hours. SAP is associated with high mortality despite the advances in its management. Herein, we report a case of SAP successfully treated with blood purification techniques on top of the current management guidelines for SAP.

CASE
A 48 year old female presented with persistent abdominal pain due to acute necrotizing pancreatitis. Her abdominal computed tomography (CT) scan demonstrated walled-off necrosis (WON) anterior to the pancreatic head and tail that extends down to the anterior compartment of the right thigh, measuring 7.6 x 7.1 x 31 cm in its widest measurable diameter. She underwent surgical drainage of the retroperitoneal abscess. Despite the broad-spectrum antibiotics, she went into septic shock and acute renal failure. We performed combined Slow Low Efficiency Dialysis (SLED) for 6 hours with blood flow rate (Qb) of 150 ml/min, dialysate flow rate (Qd) of 300 ml/min and hemoperfusion using sepsis (Jafron HA 330) filter for 2 ½ hours with Qb of 150 ml/min for three consecutive days. Her Acute Physiology, Age, Chronic Health Evaluation II (APACHE II) score improved after treatment with 12% reduction in predicted mortality rate. She also developed encephalopathy and obstructive jaundice and we performed Double Plasma Molecular Adsorption System (DPMAS) treatments using bilirubin (Jafron BS 330) and ammonia (Jafron HA330- II) filter. After three sessions of DPMAS, our patient's sensorium improved, jaundice lightened and serum bilirubin and ammonia levels significantly decreased. She was eventually discharged after successful treatment.

CONCLUSION
Blood purification therapy can be used to improve patient's survival in life-threatening conditions such as SAP.

see table/figure on following page

Laboratory Tests	Before DPMAS	After DPMAS
WBC/mm3	19280	18980
Platelet/mm3	69000	118000
SGPT (mg/dl)	98	80
SGOT (mg/dl)	157	55
Total Bilirubin (mg/dl)	25.76	6.71
Conjugated Bilirubin (mg/dl)	20.42	5.90
Unconjugated Bilirubin (mg/dl)	5.34	0.81
Partial Thromboplastin Time (sec)	63	37.3
Prothrombin Time (sec)	27.5	16.5
International Normalized Ratio (INR)	2.31	1.38
Blood Urea Nitrogen (mg/dl)	89	55
Creatinine (mg/dl)	2.99	1.45

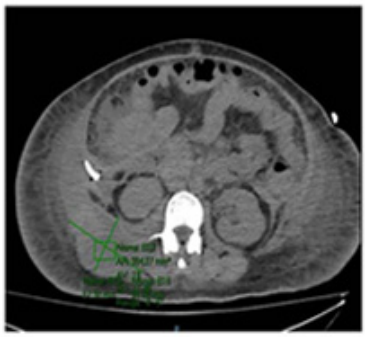

Fig. 1: Whole Abdominal scan trasverse view showing WON

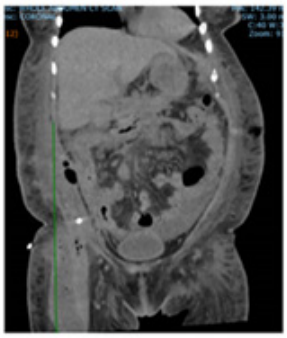

Fig. 2: Whole abdominal CT scan coronal view showing extension of WON to the anterior compartment of the right thigh

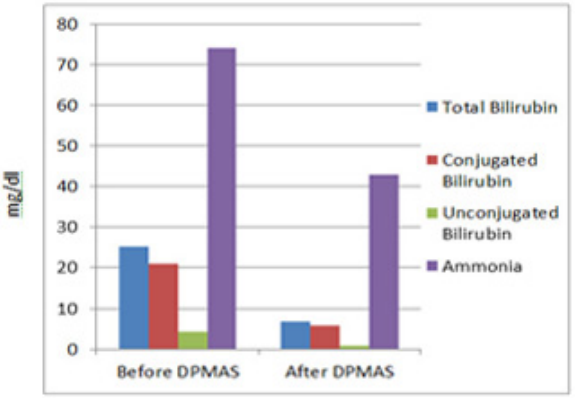

Fig. 3: Liver function tests before and after DPMAS

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Continuous Renal Replacement Therapy in a Pediatric and Oncological Hospital of Bogotá, Colombia

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[1]*Fundacion Hospital Prediatrico de la Misericordia*

Introduction. Continuous renal replacement therapy (CRRT) has been shown to be useful in critically ill patients by helping to improve problems arising from volume overload states or those caused by metabolic disturbances such as uremia or electrolyte imbalance, etc. In most third-level hospital in Bogota,these techniques are available and have become an indispensable tool in intensive care units.

Methods. We performed a retrospective observational study describing the clinical characteristics of pediatric patients receiving CRRT in the PICU of the Fundación Hospital Pediátrico de la Misericordia in Bogota, Colombia for a period of 12 months (September 2016 - August 2017). We used the Aquarius™ System technology (Nikkiso America Inc.).

Results. We report 20 children (70% men) with a mean age of 9.4 years, 45% (9/20) had a diagnosis of any kidney disease, 30% (6/20) an oncological disease and the remaining 25% had another disease. The indication for initiating CRRT was uremia (4/20), hypervolemia (4/20) or both (12/20); the glomerular filtration rate (GFR) at the beginning of therapy in uremic patients was 10.8 mL/min/1.73m2, in uremic and hypervolemic patients was 43.7 mL/min/1.73m2 and in patients only with fluid overload was 126 mL/min/1.73m2. We used HF in 13 patients (65%) and HDF in 7 (35%). The mean effluent dose was 45 mL/Kg/h (1,232 mL/m2/h), 42.7 mL/Kg/h in HF and 49.2 mL/kg/h in HDF. The mean fluid overload was 11,8%, in only hypervolemic patients was 14,3%. On average, the time between ICU admission and the beginning of CRRT was 43.9 hours (range 3-216, SD 58.1) and the duration of therapy 117,3 hours (range 16-456, SD 109). 90% of patients received citrate anticoagulation (ACD-A, Baxter Healthcare Corporation), maintaining mean serum calcium values of 1,17 mmol/L and extracorporeal calcium of 0.42 mmol/L. The ICU stay was 16.5 days (range 2-39, SD 11.6) and mortality was 40% (8/20), all of whom had septic shock including all cancer patients. Finally, patients who died had a higher percentage of hypervolemia (15.1 vs. 9.6%, $p = 0.1$), a later onset of therapy (82.6 vs. 18.1 hours, $p = 0.01$) and a slightly lower effluent dose (42.9 vs. 46.4 ml/kg/h, $p = 0.55$).

Conclusion. Based on this series of patients we concluded that CRRT are a useful therapeutic option in the pediatric population, however, in cancer patients and those with septic shock should be initiated early because delay is associated with higher mortality.

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SHOULD THE CRITERIA FOR STARTING ACUTE RRT IN ICU VS. OUTSIDE ICU BE DIFFERENT?

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INTRODUCTION: Considering that acute renal replacement therapy (RRT) should be considered when metabolic and fluid demands exceed total kidney capacity and that demand for kidney function is determined by non-renal comorbidities, severity of the acute disease and solute and fluid burden, the criteria for starting RRT in Intensive Care Unit (ICU) vs outside ICU may be different. Objective: To investigate whether criterion for starting RRT outside ICU should be different from those used for starting RRT in ICU patients. Methods: We performed a retrospective observational study that evaluated AKI KDIGO 3 adults patients underwent RRT in ICU and outside ICU from 2012 to 2018 in a teaching Brazilian Hospital. Results: We evaluated 913 adults AKI patients KDIGO3 underwent RRT, 629 (68.9%) outside ICU and 284 (31.1%) in ICU. Infections were the main cause of hospitalization (34.4%). Septic and Ischemic AKI were the main etiology of AKI (50.8% and 32.9%, respectively), metabolic and fluid demand to capacity imbalance was the main indication for dialysis (69.7%) and intermittent hemodialysis (IHD) was the method more used (59.2%). General mortality rate after 30 days was 59%.There is no difference between the two groups in gender, age and main diagnosis. The two groups were different in acute tubular necrosis index specific score (ATN-ISS), AKI etiology, elderly population, indications for dialysis, dialysis methods and mortality rate. In-ICU, patients higher 65 years old and septic AKI were more frequent (49.1 vs. 41.4% and 55.1 vs. 37.5%, respectively), while ischemic and nephrotoxic AKI were less frequent (24.3 vs. 37 and 10.2 vs. 16.3%, respectively), ATN-ISS was higher (0.74±0.31 vs. 0.58±0.16), metabolic and fluid demand to capacity imbalance as indication for acute RRT, prolonged intermittent hemodialysis (PIRRT) and continuous renal replacement therapy (CRRT) were more frequent, while peritoneal dialysis (PD) was less frequent (74.6 vs. 69.7%, 31.6 vs. 22.4%, and 5.3 vs. 17.8%, respectively) and mortality was higher (69 vs. 54.7%, respectively). At logistic regression, age, septic AKI and being in ICU were factors associated with death. Conclusions: The criteria for starting RRT in ICU vs. Outside ICU were different; however they had not impact in outcome patients.

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Effectiveness of Vasopressin inhibitor (Tolvaptan) in delaying progression of kidney disease among patients with autosomal dominant polycystic kidney disease—A Meta-analysis and Review of Literature

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Effectiveness of Vasopressin inhibitor (Tolvaptan) in delaying progression of kidney disease among patients with autosomal dominant polycystic kidney disease—A Meta-analysis and Review of Literature
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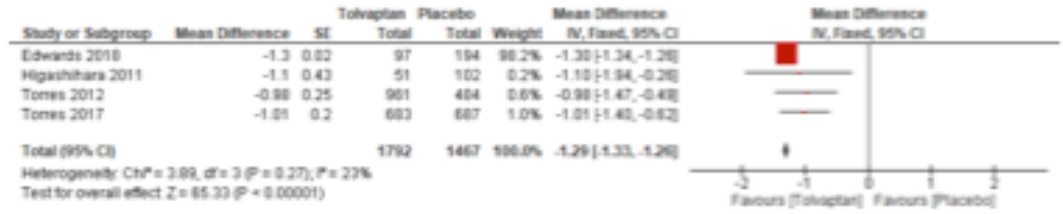
Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common hereditary kidney disease and is the fourth leading cause of end-stage kidney disease among adults. Tolvaptan has recently been approved for

delaying progression of kidney disease among ADPKD patients. This meta-analysis will look into the clinical trials which served as the basis of recommending tolvaptan in ADPKD and review other cases treated with tolvaptan. Patients diagnosed with ADPKD treated with tolvaptan and evaluated its effectiveness in terms of total kidney failure and change in eGFR were searched across databases.

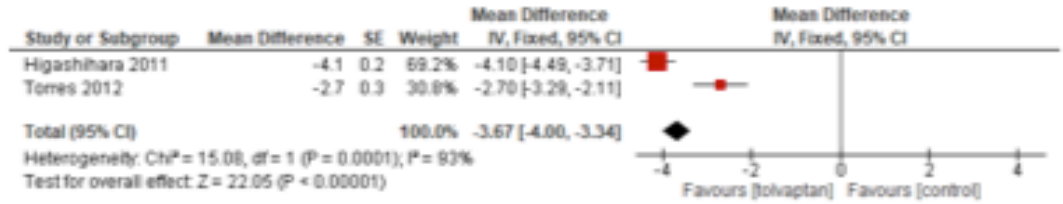
This meta-analysis aims to determine the effectiveness of tolvaptan in delaying progression of kidney disease among patients with autosomal dominant polycystic kidney disease and to summarize evidence on tolvaptan in its use in autosomal polycystic kidney disease and to present the quantitative summary through a forest plot of tolvaptan in delaying growth of total kidney volume and slowing the rate of eGFR decline among this subset of patients. After a thorough search strategy, the investigators have included four clinical trial and appraised them.

After extraction of data from these four critical trial , our meta-analysis showed that among ADPKD patients tolvaptan, albeit its cost, is beneficial in delaying kidney disease progression, the consequent need for renal replacement therapy and its associated complications, and in improving the overall quality of life. However, a major issue for the applicability of tolvaptan among ADPKD in the Philippines would be the cost. The sustainability of this therapy would be unlikely for an average Filipino. Still, this treatment option deserves merit in delaying kidney disease progression, the consequent need for renal replacement therapy and its associated complications, and in improving the overall quality of life among these subset of patients.

Forrest Plot 1. Tolvaptan in slowing the rate of eGFR decline



Forrest Plot 2. Tolvaptan in delaying growth of total kidney volume



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Therapeutic plasma exchange (TPE), Intravenous IG G, Intravenous Rituximab, as a succesfully alternative in treatment of acute humoral renal graft rejection (AHRGR).

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Therapeutic plasma exchange (TPE), Intravenous IG G, Intravenous Rituximab, as a succesfully alternative in treatment of acute humoral renal graft rejection (AHRGR).

Introduction
Acute humoral renal graft rejection is still a challenge problem. Treatment includes steroid bolus, monoclonal antibodies, plasmapheresis and, recently, therapeutic plasma exchange (TPE) which has shown good results. The aim of this report is to show our results with TPE.

Results
From 2015 to 2018, we had 5 patients with an acute humoral renal graft rejection (Table 1), they all got the requirements for AHRGR (abrupt increase of creatinine, anuria, graft pain, haematuria and ultrasound showing rejection). Four of them showed on biopsy CD4 + and tubulointersticial damage, one patient didn't have biopsy due to age and high risk.
Five patients initially got three Intravenous bolus of methylprednisolone. The first two patients did not show good results, we decided switch them to a different treatment based on recent reports, using our Prismaflex plus Gambro with TPE 2000 set, one exchange every other day, alterning conventional hemodyalisis.
Eschema
THERAPEUTIC PLASMA EXCHANGE every other day with one volume exchange
IMMUNOGLOBULINE G 500-750 mg/kg in a slow infusion immediately after TPE
RITUXIMAB intravenous 375 mg/m2 of BSA once a week for two consecutive weeks.

TABLE 1.- Patient´s characteristics
Age Sex Pretransplant diagnosis Cross Matching Donor Biopsy Treatment

26 M Tubulo Intersticial Necrosis Neg Father C4d+ TPE+ Timoglobulin
41 M Type II Diabetes Neg Cousin C4d+ Only TPE
50 F Primary Glomerulopathy Neg Friend C4d+ TPE+IV IG+ Rituximab
57 M Type II Diabetes Neg Friend No TPE+IV IG+ Rituximab
47 M Membranous Nephropathy Neg Adopted son C4d+ TPE+IV IG+ Rituximab

Two initial patients did not complete the schema and did not have good results.
Three last patients showed excellent results, increasing diuresis and creatinine clearance, keeping normal values at moment of this report.

Conclusions
Steroids are not always useful, we do not recommend it. We recommend early biopsy, and prompt starting of an aggressive treatment with PTE based on experience from the Infantil Hospital of Mexico "Federico Gomez" where they have shown very good results.

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Clinical benefit of protocol-based electrolyte-rich dialysate during continuous renal replacement therapy in the patients with acute kidney injury

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Background
Hypophosphatemia and hypokalemia occur frequently during continuous renal replacement therapy (CRRT). We evaluated the stability of serum phosphate and potassium levels between patients administered one of three types of dialysis solution and protocol.
Methods
We included 329 intensive care unit patients who were admitted for CRRT from January 2015 to December 2018. Patients were divided into three groups: group 1 (n=109) received Hemosol B0 (no potassium or phosphate) as both dialysis and replacement fluids; group 2 (n=79) received Hemosol B0 and potassium-containing solution (MultiBic); group 3 (n=141) received phosphate- and potassium-containing solution (Phoxilium), Homosol B2, Prismasol 2, and Prismasol 4. Each group also followed a different protocol.
Results
The incidence rates of hypophosphatemia and hypokalemia during CRRT were lower in group 3 patients (i.e., who received phosphate- and potassium-containing dialysis solution) compared with those in groups 1 and 2. Rates of phosphate and potassium replacement were significantly lower in group 3 compared with groups 1 and 2. Patients in group 3 experienced stable serum phosphate and potassium levels during CRRT. Serum bicarbonate, base excess, and ionized calcium levels decreased and were lower in group 3 patients compared with those in groups 1 and 2. However, no patient required additional intravenous bicarbonate and calcium replacement.
Conclusion
The use of phosphate- and potassium-containing solution reduced variability in serum phosphate and potassium. The use of an electrolyte-rich dialysis solution and an adequate protocol, based on electrolyte levels, effectively prevents episodes of hypophosphatemia and hypokalemia during CRRT.

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Effect Of Therapeutic Plasma Exchange With Membrane On Glomerular Filtration Rate In Patients With Acute Humoral Rejection

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Purpose: AMR is the main risk factor for graft loss, especially after the first post transplant year. Up to 80% of patients achieve response with immunosuppressive treatment and TPE, although the response is lower in patients with late AMR. The objective was to determine the effect of TPE on GFR at 0, 1 and 3 months postTPE.
Methods: Retrospective study that included patients with renal transplant of the CMN“November 20”ISSSTE from 2016to2019, undergoing membrane TPE for AMR. Analysis was performed using student's t or

MannWhitneyU, repeated measures analysis and Spearman or Pearson test. Significant p was less than 0.05. Results: 25 patients with AMR who received TPE were evaluated. Age:32±11.6 years, 72% from living donor, and 52% received Basiliximab. 87% received tacrolimus. 80% of AMR events were late (more than 6 months post-transplant). The GFR at the time of diagnosis was38.2±23.8 ml/min, and at discharge (0), 1 and 3 months postTPE were 43.3±24.8, 34.1±19.5, and 35.9±28.7 ml/min. Prevalence of HLA class II DSA(66%), specifically vs DQ and DR (57.2% and 28.8%). There was a significant difference between preTPE GFR and at the end of treatment(p=0.015, r=0.53). There were no significant differences when comparing the preTPE GFR, with one monthGFR(p=0.58), or after 3 months postTPE(p=0.36). When evaluating IFTA, no difference was detected in the GFR at 3 months postTPE. When analyzing the histological score(g+ptc), no differences were detected between the score obtained and the average GFR at discharge(p=0.19), one month(p=0.22) and 3 months(p=0.06) post-TPE. When comparing the effect of the AMR temporality on the GFR, difference was found at one month (p=0.01) and 3 months (p=0.022) postTPE, with a lower recovery of GFR in patients with early AMR. The response to treatment(GFR±30% from baseline at 7 days postTPE) was 60%. There was a moderate correlation between GFR at the time of diagnosis of rejection and GFR at 3 months postTPE(r2=0.68,p=0.01).
Conclusions: Significant difference was demonstrated between the preTPE GFR and the immediate postTPE GFR. IFTA did not appear to influence the GFR at 3 months. In our study patients with early AMR presented a poor response to treatment. The GFR upon admission correlated positively with the GFR detected at 3 months post-TPE. This suggests a beneficial effect of TPE over GFR fall during the first 3 months after diagnosis.

Donor Type: Male/Female (%)	72/28
AMR: Early vs Late(%)	20/80
GFR(ml/min): Basal/Pre-TPE/Post-TPE/1 month/3 months	73+/-32; 38+/-23; 43+/-24; 34+/-19; 35+/-28
Hystollogic score (g+ptc)	3.6+/-1
C4d % (positive/negative)	36/64
DSA Subtype (%)	DQ 57%, DR 28%

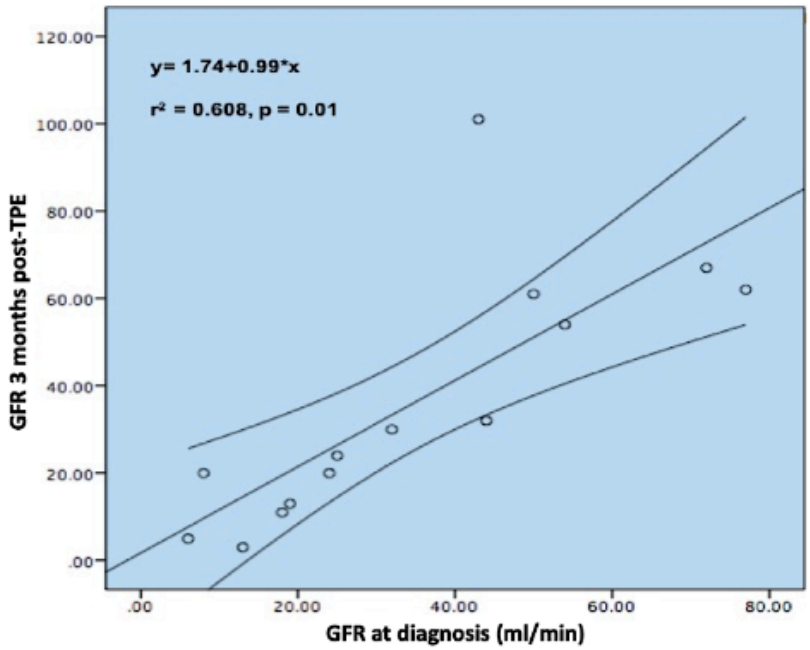

Image 1. Correlation between the glomerular filtration rate (GFR) at admission and 3 months after therapeutic plasma exchange (TPE).

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Citrate Pharmacokinetic Study in Decompensated Liver Disease Patients Receiving Continuous Renal Replacement Therapy

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Introduction: Currently, regional citrate anticoagulation (RCA) is recommended as the first line anticoagulant by Kidney Disease Improving Global Outcomes. However, little is known for the pharmacokinetic of citrate, which mainly is metabolized by liver, in the setting of decompensated liver disease. Thus, we aimed to study the citrate pharmacokinetic in decompensated liver disease patients who need continuous renal replacement therapy (CRRT).
Methods: We prospectively enrolled decompensated liver disease patients receiving CRRT in intensive care unit at Chulalongkorn Hospital, Bangkok, Thailand. We used blood flow rate of 110 ml/min and pre blood pump citrate replacement fluid was infused at a final citrate concentration of 3 mmol per liter of blood flow. We infused citrate for 2 hours and serial blood sample were obtained from arterial line from baseline until 2 hours after citrate was stopped. The filter clearance was calculated using plasma concentrations of citrate at the inlet and the outlet of the filter. The body citrate clearance was defined as subtracting total citrate clearance by filter clearance. Pharmacokinetic analysis was performed with Phoenix® WinNonlin® version 8.2 (Certara USA, Inc., Princeton, NJ).
Results: There were six decompensated liver disease patients in this study. Mean age were 59 years, with mean APACHE score of 20. Clinical diagnosis were sepsis in five patients and acute heart failure in one patients. Cause of liver failure in all patients was ischemic hepatitis and two patients had underlying cirrhosis. All patients had grade 3 or more hepatic encephalopathy with mean total bilirubin of 13.94 ± 7.4 mg/dL. Average delivered citrate doses were 19.95 mmol/h. Mean body citrate clearance were 135.4 ± 70.5 ml/min. There were decreased body citrate clearance when compared with previous study in non-liver disease critically ill patients (648 ± 347 ml/min). Mean peak concentration of citrate was 0.64 ± 0.25 mmol/L. There were two patients with serum total calcium to ionized calcium ratio more than 2.5. However, there was no major metabolic complication of citrate. One patient experienced mild hypocalcemia.
Conclusion: This is the first pharmacokinetic study to demonstrate citrate clearance in acute decompensated liver disease receiving CRRT and showed significant reduction in citrate clearance in this specific setting. Although no major metabolic complication was observed, the use RCA in these patients must be with caution.

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Use of continous renal remplacement therapy in pacients with chronic kidney disease in conventional hemodialysis in Hospital Centro Medico Nacional “20 de Noviembre”, Mexico city

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OBJECTIVE: Describe the characteristics and prognosis of patients with diagnosis of chronic kidney disease (CKD) in intermittent hemodialysis (IHD) submitted to continuous renal replacement therapy (CRRT) and it's complications during the session. Patients with CKD are admitted to the intensive care unit (ICU) with more frequency than patients with normal renal function. The main causes of admission and mortality are sepsis and cardiovascular events (CVE). In comparison with patients with normal renal function, patients with CKD have a greater risk of mortality, the greatest risk of mortality seems to stratify with comorbidities and severity. METHODS: Descriptive analysis of the quantitative and qualitative variables of patients in the hemodialysis unit that needed to be hospitalized in ICU in the period of January to December 2019. RESULTS: We evaluated a total of six patients, five women and one man, with an average age of 39.8 years (range: 14 to 70 years). The etiologies of CKD were malformation of the urinary tract, diabetic nephropathy, renal-limited vasculitis and two patients with unknown etiology for the disease. The time with CKD was 4 to 24 years, with a period in IHD of 1.5 to 12 years. Five patients presented with shock (3 patients septic shock and 2 patients cardiogenic shock) during hospitalization. Three patients were initially treated with IHD because of severe hyperkalemia. The average of treatment with CRRT was of 1.8 sessions/patient. They received 11 sessions in total, average duration of every session was 39.9 hours (12 to 57 hours). Predominant modality was continuous venovenous hemodiafiltration (CVVHDF) (72.7%). Forty five percent presented fluid overload over 10%. The prevalent venous access was the femoral Mahurkar catheter (66.6%). In 27.7% of the sessions the filter was coagulated. Just in one patient was necessary the suspension of the CRRT because of refractory hypotension. Three patients (27.27%) died. Three patients went back to the chronic hemodialysis program of the institution. CONCLUSIONS: The causes of admission (sepsis and cardiovascular events) were concordant with the findings of Manhes et al. and Uchino et al. Juneja et al. identified the necessity of mechanical ventilation and/or vasopressor aid as predictor of negative results in the ICU and Sood et al. discovered that the principal factor in mortality was the severity of the disease, concordant with the fatal result of three of our patients.

Demographic characteristics

Gender	Age (y)	Etiology	Time ESRD (y)	Time IHD (y)	Diagnosis	APACHE II (%)[6]	SOFA (%)[6]	# Sessions	Indication CRRT	Type CRRT	Duration (hrs)	Withdrawal CRRT	Access	Dead
F	14	Malformations GUT	7	3	Septic shock	32 (75)	15 (>80)	4	Uraemia + FOD	CVVHDF[1]	38.25*	Filter coagulation[4]	Femoral[3]	No
F	33	Unknown	15	12	Septic shock	39 (85)	17 (>90)	1	FOD	IHD + SCUF	45	Improvement[5]	Intracavitary	No
M	59	Unknown	24	5	Cardiogenic shock	35 (85)	15 (>80)	2	Uraemia	CVVHDF[1]	53*	Improvement[5]	Arteriovenous fistula	Yes
F	37	Diabetic nephropathy	6	3	Septic shock	31 (75)	15 (>80)	2	FOD + Uraemia	SCUF // CVV	50.5*	Improvement[5]	Femoral[3]	Yes
F	70	Diabetic nephropathy	4	1.5	Cardiogenic shock	33 (75)	15 (>80)	1	Uraemia	CVVHDF	12	Filter coagulation[4]	Femoral[3]	Yes
F	26	Renal vasculitis	13	7	Acute pulmonary edema	26 (55)	11 (40-50)	1	FOD	IHD+SCUF	22	Filter coagulation[4]	Femoral[3]	No

(1) All sessions
(2) Second session
(3) Non-tunneled catheter
(4) One session
(5) Clinical and biochemical improvement
(6) Score (mortality)
*Average

ESRD: End Stage renal disease
CRRT: Continuous Renal Replacement Therapy
FOD: Fluid overload
IHD: Intermittent Hemodialysis
CVVHDF: Continuous Venovenous Hemodiafiltration
SCUF: Slow Continuous Ultrafiltration
GUT: Genitourinary malformations

APACHE II: Acute Physiology And Chronic Health Evaluation II
SOFA: Sequential Organ Failure Assessment

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High Volume Hemofiltration may Prevent the Need of Extracorporeal Membrane Oxygenation in Patients with Severe Hantavirus Cardiopulmonary Syndrome.

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Andes Hantavirus produces a spectrum of clinical pictures, from dry caugh to a severe disease characterized by respiratory failure due to capillary leak into lung interstitium and profound myocardial depression. High fever, severe metabolic acidosis, low platelet count and AKI, are usually associated. This entity is referred to as Hantavirus Cardiopulmonary Syndrome (HCPS). Treatment is mainly supportive, with mechanical ventilation, vasoactive drugs and extracorporeal circulatory support with venous-arterial membrane oxygenation (VA ECMO) as main managements. High volume hemofiltration (HVHF) has been used to support patients with septic shock and it has been anecdotally used in patients with HCPS. We hypothesized that HVHF could allow homeostasis correction by controlling hyperthermia, metabolic acidosis without fluid overload and modulation of the inflammatory response, eventually preventing the necessity of VA ECMO.
We retrospectively analyzed a cohort of five patients (age 15 to 29 years) with severe HCPS, connected to mechanical ventilation and under drugs support, that were submitted to HVHF (> 50 ml/kg/h of convective depuration plus ultrafiltration to maintain fluid balance). We considered that the patients responded to therapy if VA ECMO was not needed as additional support.
Patients were similar in disease severity (higher SOFA score 12, range 10-14). All had severe myocardial depression (average lower cardiac index 2.07 L/min/m2, average Stroke Index 31.8 mL/m2) and respiratory failure (lower PaO2/FiO2 ratio 162). Three patients reached the endpoint while the other 2 had to be VA ECMO supported. Responders stayed fewer days in mechanical ventilation(3 vs 9.5 days). A main difference between groups was time span between intubation and connection to HVHF, being shorter in responders 15.3 vs 22.5 h). Bicarbonate infusion and net negative fluid balance were also higher in responders. One of the 2 patients in ECMO experienced vascular complications due to the treatment. All patients survived.
We conclude that HVHF, used early in the evolution of severe HCPS, may support the patients, correct metabolic complications, shorten mechanical ventilation and prevent the need of more complex support measures such as VA ECMO.

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Use of BNP as Quantitative Marker of Fluid Overload in Neonatal RRT

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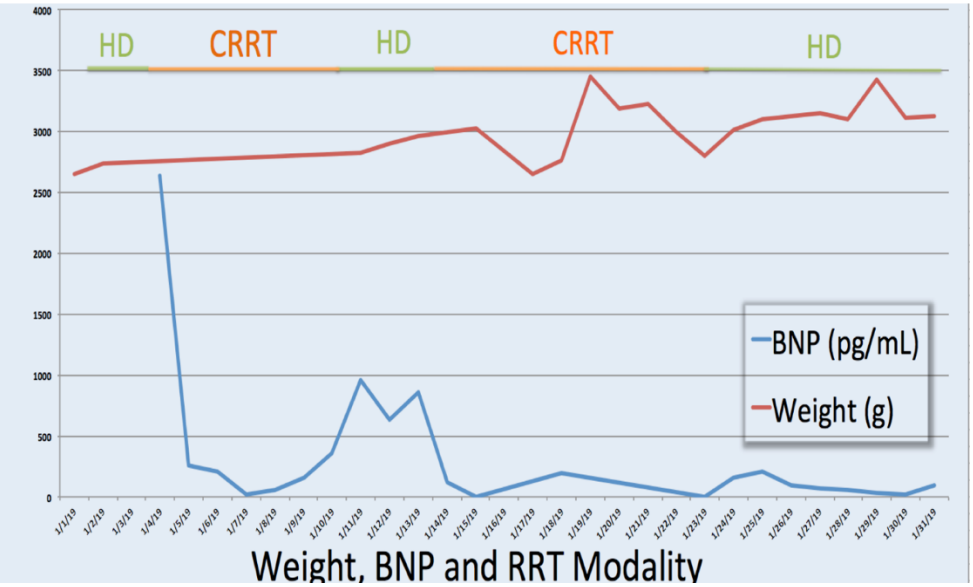
Purpose of the Study:
Neonatal renal replacement therapy (RRT) remains one of the most challenging scenarios in Pediatric Nephrology. Evaluation of dry weight can be particularly difficult as fluid overload may be mistaken for adequate nutritional weight gain. Physical exam is insensitive in assessing hypervolemia until the patient has developed significant fluid overload. Non-invasive BP measurements are problematic as upper extremities are often used for intravenous access and patient cooperation/degree of sedation alters measurement. B-type natriuretic peptide (BNP) has long been used in the evaluation of heart failure and has even been utilized as a marker of fluid overload in adult hemodialysis patients, but its role has been questioned due to co-morbidities of cardiac disease and heart failure in adults. The purpose of our study was to evaluate the role of BNP as a quantitative marker of fluid overload in a neonate with end-stage renal disease.
Case Study/Methods
Term baby girl with bilateral renal agenesis requiring emergent RRT after birth.
BNP via chemiluminescent microparticle immunoassay (CMIA) was utilized as a quantitative marker of fluid overload.
Following the failure of peritoneal dialysis due to peritoneal leak, this 2.19 kg child was transitioned to hemodialysis (HD). Despite daily 3 hr HD treatments with ultrafiltration (UF) goals guided by weight, physical exam findings and blood pressure, patient developed bilateral pulmonary edema and cardiomegaly at 3 weeks old. BNP was found to be > 5,000 pg/mL and RRT modality was changed to continuous veno-venous hemodiafiltration (CVVHDF). BNP normalized after 4 days of CVVHDF, but upon transition to HD and without use of BNP, she again developed fluid overload and required placement back on CVVHDF. Thereafter, BNP was utilized as a quantitative marker of fluid overload with UF goal guided by pre- and post-dialysis BNP levels. Utilizing this technique, the patient had no further episodes of fluid overload (see figure).
Conclusion:
In this low birth weight infant with no pre-existing comorbidity, serial BNP measurements allowed for an objective assessment of volume status and showed superiority in assessing fluid balance over weight and blood pressure variance. BNP appears to be a promising additional tool in assessing fluid status in pediatric RRT. A formal study on BNP in infants to confirm these findings is currently being investigated.



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Use of Continuous Renal Replacement Therapy (CRRT) in Special Situations. Case Report.

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The purpose of this paper is to present the case of a critically ill pediatric patient, who developed multiple organ failure, including acute kidney injury (AKI) with continuous renal reemplacement therapy (CRRT) requirement, who after a series of appropriate hemodialysis sessions and medical management, resolved the renal failure, being discharged from critical area with renal function in basal ranges.
This is a 15-year-old male patient, with no relevant medical history, who began his condition with spontaneous deviation of the labial commissure, managed with steroids, without improvement. Subsequently, intense headache was added and 3 days later generalized tonic-clonic seizures. Magnetic resonance study (July 07th, 2019) reported cerebral parenchyma with loss of morphology at the left frontotemporoparietal hemisphere, secondary to lesion of well-defined borders, dimensions 73.2 * 81.1 * 75.7 mm. He was referred to the “Centro Médico Nacional “20 de Noviembre”” to continue diagnostic approach and treatment. He was assessed by neurosurgery, integrating the diagnosis of meniongioma and deciding its surgical management, requiring three surgical interventions to achieve resection of the lesión. He stayed during 22 days in critical care unit, and was discharged to hospitalization pediatric ward for improvement of his general conditions. However, he developed fever, tachycardia and polypnea, and subsequently hemodynamic and respiratory failure, requiring entering the pediatric intensive care unit again. Presenting with a torpid evolution, the patient developed multiorganic failure. He was assessed by the nephrology department for oligoanuric AKI, severe metabolic acidemia and hyperkalemia. He initiated renal replacement therapy (RRT), and received the first session of conventional hemodialysis, resolving dialysis urgency. However, the patient developed greater hemodynamic instability, oligoanuria and water overload of 7.5 liters (15% body weight), so he was considered a candidate for CRRT, modality continuous venovenous hemodiafiltration (CVVHDF). However, with a first session duration of 5 hours due to filter coagulation. Assessed the next day, it was decided to start a new CRRT session, with the same prescription parameters, urea sieving-coefficient at 24 hours of 1. After 27 hours of treatment, the patient presented a 2-minute cardiorespiratory arrest, so the CVVHDF session was terminated, quantifying at the end a total ultafiltration of 1975 ml.

NEW TECHNOLOGY

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Extracorporal Cytokine Adsorption: Significant Reduction of Catecholamine Requirement in Patients with AKI and Septic Shock After Cardiac Surgery

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Purpose:
Extracorporal cytokine adsorption is a new option in septic shock as an additional measure to prevent severe cytokinaemia. Purpose of this study was to investigate the effects of extracorporal cytokine adsorption on hemodynamics in patients with AKI and septic shock after cardiac surgery.

Methods:
In this retrospective study 64 patients with septic shock and AKI after cardiac surgery were investigated for the effect of extracorporal cytokine adsorption by CytoSorb® on hemodynamics. All patients were on CRRT with citrate anticoagulation during CytoSorb®-treatment. A paired t-test has been performed to determine statistical significance.

Results:
58 % of the patients were male, 42 % female, the average age was 67 years (range 46-83 years). 54 out of 64 patients (84 %) had a pneumosepsis. CytoSorb ®-treatment was 15-40 h with 1 to 4 adsorbers used per patient. Before treatment, the mean noradrenalin dose to reach a MAP > 65 mmHg was 0.49 µg/kg bw/min, the mean adrenalin dose was 0.1 µg/kg bw/min. 24 h after treatment, significantly reduced catecholamine doses were necessary to maintain a MAP > 65 mmHg (0.23 µg/kg bw/min noradrenalin; $p^* < 0.0002$ and 0.06 µg/kg bw/min adrenalin; $p^* < 0.02$). The mean SOFA-score for these patients with septic shock and AKI 24 h before Cytosorb®- treatment was 16.6 points. The mean predicted in-hospital mortality rate based on this SOFA-score of 16.6 points was 77 % (Raith et al., JAMA 2017) while the all-cause mortality rate of the patients in this study was 59.4 %.

Conclusion:
In patients with septic shock and AKI after cardiac surgery, 24 h after extracorporal cytokine adsorption by CytoSorb® the catecholamine dose required to maintain a MAP > 65 mmHg was halved. Additionally, observed versus SOFA-score predicted in-hospital mortality rate was decreased.

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Development and Validation of a Computable Phenotype to Identify and Characterize Kidney Health in Adult Hospitalized Patients

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Purpose: The kidney health of any patient can be characterized by the presence of chronic kidney disease (CKD), any acute kidney injury (AKI) and any recovery from that injury, with these conditions staged using consensus clinical criteria. We developed and validated an electronic phenotype to identify and stage CKD, AKI and AKI recovery in adult hospitalized patients using an integrated clinical database.
Methods: We used the University of Florida Integrated Data Repository to develop, validate and test the phenotype. This database includes demographic information, clinical data and diagnosis and procedure codes. We developed a single algorithm to identify CKD, AKI and AKI recovery based on Kidney Disease: Improving Global Outcomes (KDIGO) and Acute Disease Quality Initiative (ADQI) criteria. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the CKD and AKI diagnoses produced by the algorithm were compared to clinical adjudication of CKD and AKI performed by clinician experts on 300 selected cases.
Results: In a validation cohort of 71,127 patients approximately 48% of the population were male and the mean age was 56 years old. The algorithm identified CKD of any stage in 16.9% of the admissions in the cohort, and 17.5% had stage G1, 32.1% had stage G2, 39.6% had stage G3, 8.2% had stage 4 and 1.6% had stage G5. The algorithm identified AKI of any stage in 20.8% of the patients, with 62.8% stage 1, 19.3% stage 2 and 17.8% stage 3 AKI. For those patients with AKI 62.3% developed persistent AKI while 37.7% had rapidly reversed AKI. For CKD the PPV of the algorithm was 0.87 (95% CI 0.81-0.92), the NPV was 0.99 (95% CI 0.96-1.00), the sensitivity was 0.99 (95% CI 0.96-1.00) and the specificity was 0.89 (95% 0.83-0.93) compared to chart review. For AKI the PPV of the algorithm was 0.99 (95% CI 0.96-1.00), the NPV was 0.95 (95% CI 0.89-0.98), the sensitivity was 0.98 (95% CI 0.94-0.99) and the specificity was 0.98 (95% CI 0.93-1.00) compared to chart review.
Conclusions: We developed an electronic phenotype for kidney health that shows excellent performance in identifying patients with CKD and AKI in an integrated clinical database. This tool may be useful in identifying patients with kidney disease in a large population, in assessing the quality and value of care provided to such patients and in clinical decision support tools to help providers care for these patients.

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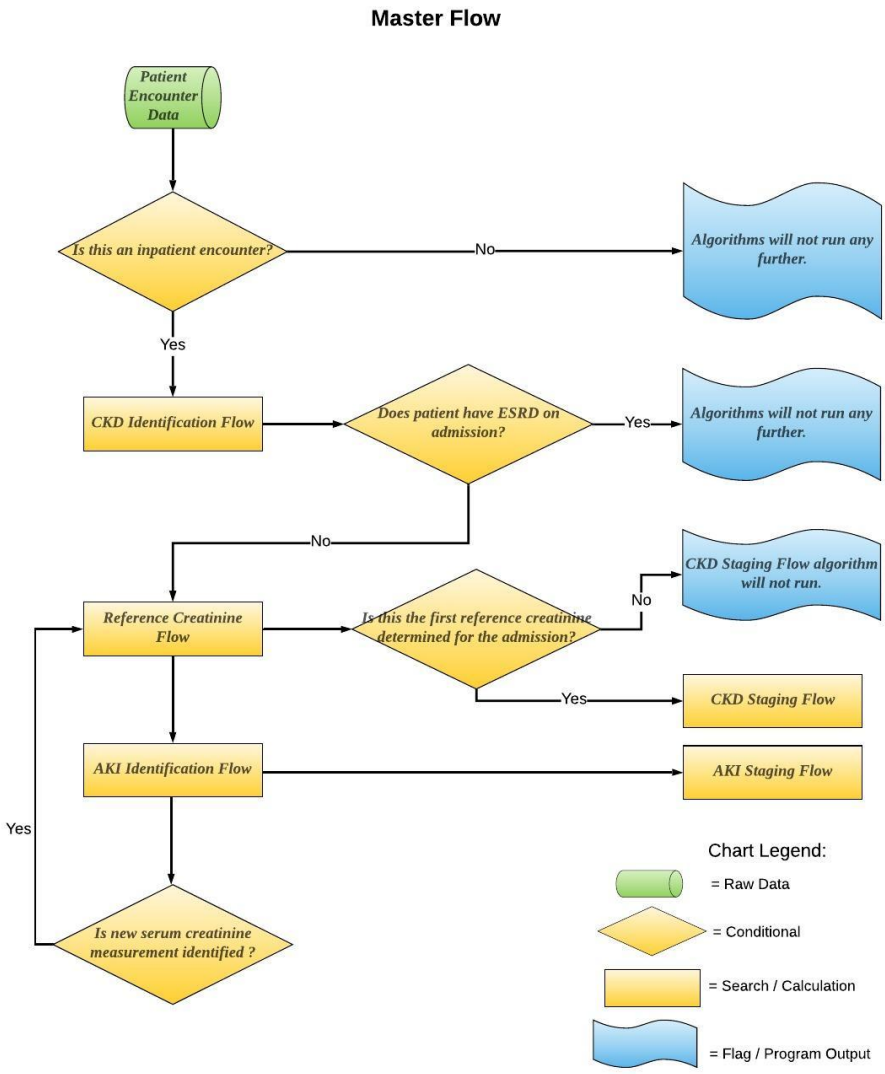

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Usefulness of Polymyxin B Hemoperfusion in the Patients with Septic Acute Kidney Injury Requiring Continuous Renal Replacement Therapy

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Background

Polymyxin B hemoperfusion (PBH) may improve clinical outcomes in the septic patients with gram-negative bacteremia by reducing endotoxin level. However, it is unclear that PBH improves the survival rate in those patients in the recent studies. These results may be explained by the fact that moderate to severe renal dysfunction is highly prevalent in them. Therefore, we investigated whether adding PBH to continuous renal replacement therapy (CRRT) could improve survival rate, compared with CRRT alone, in them.

Methods

In this retrospective study, 231 septic patients underwent CRRT alone (n=155, M:F=91:64, age 67±14 years) or PBH with CRRT (n=76, M:F=44:32, age 60±15 years). The additional initiation of PBH was determined by the intensivist. Demographic data and biochemistry parameters were obtained by reviewing electronic medical records at the initiation of CRRT in CRRT alone group or PBH in PBH with CRRT group. Primary outcomes were 28-day and 90-day all-cause mortality from then.

Results

There were no significant differences between two groups in urine output (0.56±0.87 vs. 0.74±1.23 ml/Kg/h), ventilator use (89% vs. 85.5%), and SOFA score (14.1±2.6 vs. 13.7±4.1). Although the crude 28-day and 90-day mortality rate were higher in the PBH with CRRT group compared with those of CRRT alone group (Table), inotropic score was significantly higher in the PBH with CRRT group (27.1±21.6 vs. 51.1±33.6, $p<0.05$). In order to correct disease severity, propensity score matching was performed with mean arterial pressure, inotropic score, and SOFA score. Mantel-Cox regression analysis of 49 propensity score matching pairs revealed still significantly higher 28-day and 90-day mortality rate of the PBH with CRRT group compared with those of CRRT alone group (Table).

Conclusion

Considering the mortality rates in this study, the additional use of PBH to CRRT does not seem to be effective in the improvement of clinical outcome in the septic patients with AKI requiring CRRT. In the future, randomized interventional trial is necessary whether the additional use of PBH to CRRT could improve the survival in them.

		CRRT only	PBH-CRRT	p-value	Risk Ratio	95% CI
Crude	28-Day	60/155 (38.7%)	40/76 (52.6%)	0.007	1.74	1.17-2.60
Crude	90-Day	81/155 (52.3%)	46/76 (60.5%)	0.033	1.48	1.03-2.13
Propensity-matching	28-Day	20/49 (40.8%)	28/49 (57.1%)	0.026	1.93	1.08-3.44
Propensity-matching	90-Day	22/49 (44.9%)	30/49 (61.2%)	0.025	1.88	1.08-3.27

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Regional citrate anticoagulation vs. no-anticoagulation for continuous venovenous hemofiltration in patients with liver failure and increased bleeding risk: a retrospective case-control study

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[1]*the Department of Nephrology, Xijing Hospital*

Background: There are controversial opinions on anticoagulation for continuous venovenous hemofiltration (CVVH) in patients with liver failure (LF) and increased bleeding risk. Therefore, we conducted a retrospective study to evaluate the efficacy and safety of regional citrate anticoagulation (RCA) versus no-anticoagulation for CVVH in LF patients with increased bleeding risk.
Methods: The included patients were divided into RCA and no-anticoagulation group according to the anticoagulation strategy they accepted for CVVH. Filter lifespan, bleeding, citrate accumulation, catheter occlusion, and serum total calcium / ionized calcium (totCa/ionCa) ratio were evaluated as outcomes. Additionally, patients in the two groups were matched according to the course of LF (acute/chronic) and the degree of LF.
Results: Of the 103 included patients, 41 (79 filters) accepted RCA-CVVH and 62 (162 filters) accepted no-anticoagulation CVVH. The filter lifespan of the RCA group was significantly longer than the no-anticoagulation group (> 72 hours vs 39.5 hours (IQR 31.2 - 47.8), P = 0.002). The adjusted results demonstrated that RCA could significantly reduce the risk of filter failure (HR = 0.459, 95%CI 0.26-0.82, P = 0.008). Four episodes of totCa/ionCa > 2.5 were observed in the citrate group. All of the patients with totCa/ionCa > 2.5 continuously accepted RCA-CVVH with reduced citrate dose and blood flow. No obvious citrate accumulation was observed in these patients. In the matched cohort, the filter lifespan of the RCA group was significantly longer than the no-anticoagulation group (P = 0.013) as well. No significant difference in the episodes of totCa/ionCa > 2.5 was observed between the two matched groups (P = 0.074). Both in the original cohort and the matched cohort, the bleeding, acidosis, alkalosis, and catheter occlusion incidences were not significantly different between the RCA group and the no-anticoagulation group.
Conclusions: In LF patients with increased bleeding risk who underwent CVVH, RCA could prolong the filter lifespan and be safely used with careful blood gas monitoring and citrate dose adjusting. Further prospective, randomized, control studies are warranted to obtain robust evidences.

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Study of Dilution Modes and Transmembrane Pressure under Different Operational Conditions in CVVH

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Introduction: The CRRT dose trial (Ronco et al,) was performed in the post-dilution (Post) CVVH mode. Other dose/outcome trials used different CRRT modes which may influence MM clearance. The purpose of this experimental CVVH study was to measure the clearances of small molecule (SM) solutes (urea, creatinine), MM surrogates (vancomycin, inulin) and the transmembrane pressures (TMP) in different dilution modes, degree of (Pre), and 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. But in Pre and PBP the TMP values are much lower than that in Post. 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. Longer experimental times are necessary to further understand the potential degradation in clearance over clinically relevant durations.

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Creation of a Critical Care Nephrology Research Database for Hospitalized Pediatric and Adult Patients

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Study Purpose
Our goal was to create a research database for pediatric and adult patients that would automatically gather data from the electronic health record for research and quality improvement work.

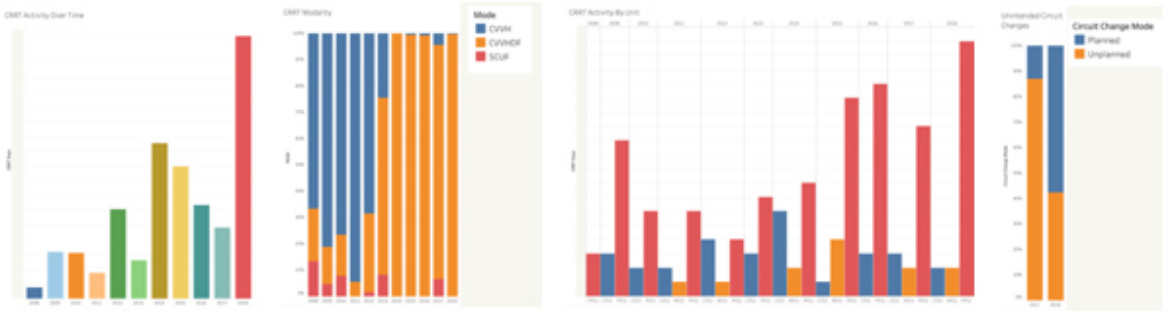
Methods
Health Data Compass (HDC) is sponsored by Children's Hospital Colorado (CHCO) and UCHealth (UCH) at the University of Colorado and has the ability to extract variables to from the electronic health record (EHR) for research purposes. We obtained IRB approval to extract de-identified patient data on any patient hospitalized at either CHCO or UCH meeting KDIGO Acute Kidney Injury (AKI) criteria. If no baseline serum creatinine (SCr) is available within 180 days of index admission, a normal SCr is back-calculated utilizing the bedside Schwartz equation for pediatric patients or first SCr measured during admission for adult patients. Data is extracted monthly with a waiver of informed consent. Patients receiving renal replacement therapies are further identified by the presence of dialysis-specific orders. Enrolled Colorado residents are linked to state records of death certificates enabling tracking of post-discharge mortality. HDC serves as an honest broker and any future research studies requiring protected health information must secure separate IRB approval. Veracity of the data pull was performed manually by HDC on a selection of patient records from 2016. Data is available from the time of implementation of the EHR system in 2007.

Results
2,365 variables were coded to pull from EHR for each patient and collated from index admission onward. Table 1 shows the main categories of information pulled, the number of variables in each category, as well as examples. Selected high-yield data have been compiled into a Visual Dashboard (Tableau) for report-out to key-stakeholders (Figure 1). Data can be filtered (i.e. pediatric vs adult, month, unit, anti-coagulation, co-morbidities) to display trends of specific interest.

Conclusions
We have created a Critical Care Nephrology Database that assembles de-identified information on patients with AKI, with or without requirement of dialysis. The database includes pediatric and adult patients and enables outcomes research as well as quality improvement initiatives.

see figure on following page

Category	# of variables pulled from EHR	Examples
Demographics	17	Age, gender, race, unit, primary diagnosis
Vitals/Severity of Illness	44	Weight, blood pressure, urine output
Co-morbidities	2,187	Chronic kidney disease, hypertension, fractures
Dialysis specific	61	Modality, prescribed dose, delivered dose
Laboratory Values	39	Serum creatinine, cystatin C, urine NGAL
Medications	78	Nephrotoxins, pressers, immunosuppressants



Example dashboard showing (left to right): number of CRRT days per year, choice of modality over time; CRRT days per unit over time; and planned versus unplanned circuit changes over time.

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Prolonged Exposure to Continuous Renal Replacement Therapy in Patients with Acute Kidney Injury and Kidney Recovery

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Purpose
CRRT remains a common modality in critically ill patients with AKI and hemodynamic instability. While the decision to initiate CRRT might be less ambiguous, termination of CRRT is usually left to clinical judgment. The purpose of this study is to assess the association of the duration of CRRT and renal recovery in patients with AKI.

Methods
This is a historical cohort study of patients with AKI admitted to the ICUs at a tertiary care hospital from 12/2006 to 11/2015, who received CRRT. The primary outcome was doubling of serum creatinine or need for dialysis at 90 days after CRRT. We excluded patients who had CRRT<1 day, those who died while still receiving CRRT, and patients who died within 90 days of CRRT initiation. We defined prolonged CRRT duration if patients required CRRT for > 7 days.

Results
Among 1,398 screened patients, 465 met the eligibility criteria. There were 143 (31%) patients who required CRRT for >7 days. Patients who received CRRT for <7 days had lower SOFA score at the time of CRRT initiation (11.1 vs. 11.8, p .04) and were more likely to remain intubated for the duration of CRRT (26% vs 12.5%, p .002) compared to patients who received CRRT for >7 days. Patients who received CRRT for <7 days had higher average daily urine output (1.2 vs. 0.5 L, p<.001)and higher net negative cumulative fluid balance(-3.6 vs. -1.1 L, p .03) during the duration of CRRT when compared to the average daily urine output or cumulative fluid balance in the first 7 days of CRRT administration in patients who received prolonged CRRT. There was no difference between the two groups in age, BMI, sex, APACHE III scores, number of vasopressors during ICU stay, baseline serum creatinine and rates of liberation from vasopressor support while on CRRT. In multivariate logistic regression, prolonged duration of CRRT was associated with increased risk of doubling of serum creatinine or dialysis at 90 days (OR: 2.6, 95%CI: 1.5-4.4, p<.001), after adjusting for age, baseline serum creatinine, SOFA score and number of vasopressors during ICU stay.

Discussion
In patients who remained alive for 90 days after receiving CRRT, prolonged CRRT duration was associated with less chance of kidney recovery. While the need for organ support (including CRRT)might be a marker of the persistence of the critical illness, the optimal duration of CRRT remains a challenging question. Further studies are required to develop guidance on how to approach the discontinuation of CRRT.

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Factors affecting circuit life during prolonged intermittent renal replacement therapy

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Purpose
The study was conducted to explore factors affecting circuit life during prolonged intermittent renal replacement therapy (PIRRT) in order to provide the basis for further quality improvement .
Method
Adults who received PIRRT made by the nephrologist in Peking University First Hospital from January 2017 to December 2017 were retrospectively reviewed. Patient and circuit factors associated with circuit lifespan were evaluated.
Result
82 patients (median age 64 years) underwent PIRRT, of which 27 (32.9%) died. A total of 898 circuits were finally included. 259 circuits (28.8%) were changed before the scheduled time (defined as the unscheduled group) with the circuit blockade being the main reason (212 circuits). Compared to the scheduled group, the unscheduled group was more likely to have no anticoagulation (34.7% vs 13.3%, $P < 0.001$), and to use femoral catheters (68.3% vs 59.8%, $P = 0.010$) and non-cuffed catheters (61.0% vs 49.3%, $P = 0.001$) as the access. Lower blood flow [(183±11)ml/min vs (187±14) ml/min, $P = 0.001$] and shorter treatment duration[(6.3±3.2) h vs (8.7±3.2) h, $P < 0.001$] were also observed in the unscheduled group. There were no significant differences in age, sex, comorbidities, the patient-nurse ratio between the two groups.
Conclusion
Circuit blockade caused by inappropriate anticoagulation, catheter malfunction and high filtration fraction might be the main factor affecting circuit life during PIRRT in the author's center.

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CRRT DOSE PREDICTOR, A NOVEL APP TOOL

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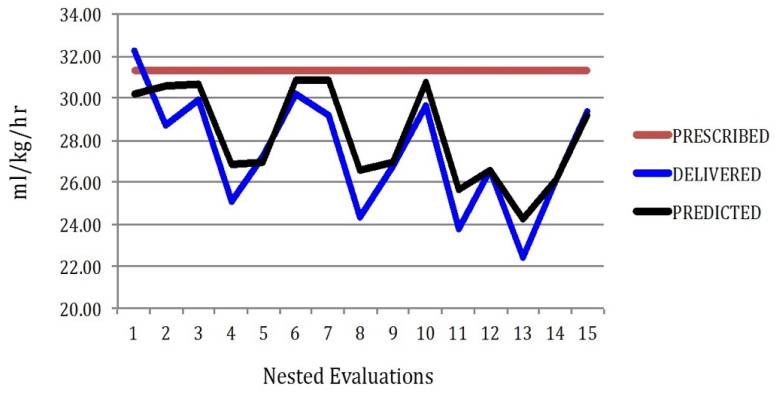
PURPOSE: Managing continuous renal replacement therapies (CRRT) involves above many other things: choosing a type of anticoagulation, prescribing a dose according to modality and measuring a real delivered dose targeted for the physiological needs of patients. All of the previous issues have made CRRT complex to understand, prescribe, evaluate and predict. The development of a simple, accurate, and accessible tool that could do this could be of great value for clinicians in contact with CRRT.

METHODS: We developed a free APP for iphone and ipad (Adequator®) that includes three CRRT calculators: 1) a dose predictor that calculates a delivered dose when given a desired therapy, 2) a measured delivered dose calculator and 3) a regional citrate anticoagulation calculator. For validation of the simulator we evaluated 15 CVVHDF treatments, and ran 50 dose evaluations by collecting effluent volume and measuring simultaneously: BUN pre-filter pre-dilution, BUN pre-filter post-dilution, and UN of the effluent. Then we compared the measured delivered dose with the results of the predicted delivered dose.

RESULTS: For prediction of dose, we used our institution average down time (2.2 hrs), a 99% effluent saturation, and the prescribed volume of pre-dilution replacement. We found a good correlation with the measured delivered dose (Pearson correlation: r =0.87, 95% CI= (0.79 - 0.92), R2=0.77) Agreement was also good (Bland Altman: Bias= 1.4, SD of Bias 2.0, 95% LA (-2– 5.5) of the difference. For simulation of dose, we use retrospectively the actual down time and effluent saturation for every dose evaluation, finding almost perfect correlation and agreement (Pearson correlation: r =0.98, 95% CI= (0.97 - 0.99), R2=0.96, Bland Altman: Bias= 0.4, SD of Bias 1, 95% LA (-1.5– 2) of the difference).

CONCLUSIONS: The Adequator® can predict accurately the delivered dose before the treatment is given to a patient. It can also accurately simulate different doses by changing prescription, modalities, down time, and effluent saturation. The measured delivered dose calculator and the regional citrate anticoagulation calculator showed to be useful for calculating actual delivered dose and initial citrate infusion rates. The use of the three calculators can be very handy in the every day monitoring, prescribing and teaching of CRRT.

Comparison of prescription, delivered and predicted dose in one treatment



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Micronutrient Deficiencies in Patients Being Evaluated for Liver Transplantation While Receiving Continuous Renal Replacement Therapy: A Retrospective Review

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Background: Continuous renal replacement therapy (CRRT) is an effective alternative renal replacement therapy (RRT) in critically ill patients with acute and chronic renal dysfunction. A consequence of CRRT is marked losses of macro and micronutrients during this therapy which may result in decreased patient survival and undesirable clinical and metabolic disturbances. To date, there is limited data exploring the incidence of vitamin and trace element deficiencies, replacement therapy, and how to adequately monitor these high risk patients for deficiencies.
Methods: A retrospective chart review was completed on patients who were being evaluated for liver transplantation from May 2019 through November 2019 at Keck Medical Center of USC. Patients who had at least 1 micronutrient level drawn (thiamine, pyridoxine, zinc, copper, vitamin C, selenium) within 48 hours of starting CRRT were included in this study. All patients were prescribed a renal vitamin or multivitamin with mineral tablet on admission to the unit.
Results: Patient's micronutrient panel were drawn within 48 hours of starting CRRT. 58 patients were included in the study. A total of 20/55 (36.7%) had low whole blood thiamine levels, 34/54 (63.0%) had low serum pyridoxal 5'-phosphate levels, 35/50 (70.0%) had low serum vitamin C levels, 28/53 (52.8%) had low copper levels, 39/53 (73.6%) had low zinc levels, and zero patients had low serum selenium levels. 2/58 (3.4%) patients did not have any altered micronutrient levels.
Conclusions: High dose vitamin and trace element supplementation may be needed routinely in patients starting CRRT as deficiencies are seen as early as within 48 hours of initiating CRRT. Large prospective studies are needed to explore the incidence of vitamin and trace element deficiencies, identify best practice monitoring strategies of patients on CRRT, determine if prophylactic micronutrient supplementation is needed, and compare micronutrient losses between different RRT modalities.

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The relationship of serum phosphorous level and arteriovenous fistula dysfunction in maintenance hemodialysis patients

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Background: It is known that maintenance of function of arteriovenous fistula (AVF) is very important in the management of hemodialysis (HD) patients. Therefore, identifying a risk factor for decreased vascular access flow has a clinical relevance in real world practice. Although hyperphosphatemia plays a crucial role in the pathogenesis of vascular calcification, there is lack of studies evaluating the effect of hyperphosphatemia on AVF. This study investigated the impact of serum phosphorous (P) on vascular access flow in HD patients

Method: Sixty-two maintenance HD patients who visited dialysis unit of Bundang CHA Medical Center from November 2016 to December 2017 were included in this study. Serum P levels were determined every month and time-averaged serum P was calculated. All patients had left arm AVF (side to side anastomosis) and vascular access flow was assessed by Transonic HD 03. Decreased vascular access flow was defined as less than 600 mL/min.
Result: The mean age was 57.9 ± 12.1 years, 32 patients (51.6%) were men. The mean serum P levels were 5.1 ± 1.1 mg/dL and the vascular access flow was 1,071.4 ± 504.2 mL/min. Decreased vascular access flow was observed in 14 of 62 patients (22.6%). In univariate analysis, higher serum P was significantly associated with decreased vascular access flow (odds ratio [OR]=2.089, 95% confidence interval [CI]=1.159-3.766, P=0.014). But there was no significant association of dialysis blood flow rate, ejection fraction on echocardiography and serum calcium (Ca) levels with vascular access flow. Multivariable analysis indicated that higher serum P was independently associated with greater risk of decreased vascular access flow (OR=4.012, 95% CI=1.651-9.711, P=0.002). Old age, reduced EF, low dialysis blood flow rate and higher serum Ca was not associated with vascular access flow.
Conclusion: This study demonstrated that higher serum P was the independent risk factor for decreased vascular access flow in maintenance HD patients. Serial monitoring of serum P may be helpful to stratify the risk of vascular access dysfunction in these patients.

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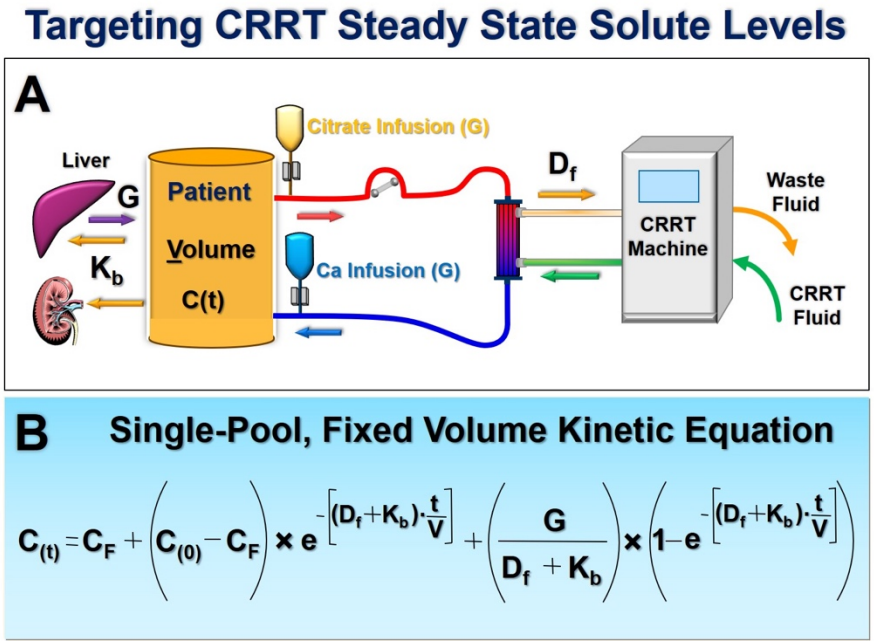
CRRT Clinical Goal Prescribing With Web Application Translation Into CRRT Settings

Balazs I Szamosfalvi[1], Lenar T Yessayan[1]

[1]*University of Michigan, Division of Nephrology*

Introduction: We describe a new approach to post-dilution CVVHDF-RCA prescribing that allows safe use of this technique by non-experts without contraindication and with optimized chance of achieving desired clinical outcomes without complications.
Body: Every time a patient is started on CRRT-RCA a very complex solute kinetic "experiment" is initialized as shown in the Figure, Panel A with multiple factors contributing in an variable and unpredictable manner, e.g. liver metabolism of citrate. The level of any specific solute as a function of time, C(t) can only be described with clinically sufficient accuracy by using a kinetic equation as shown in Panel B. The kinetic volume V, solute generation rate G, solute dialysance D(f), solute body clearance K(b) are defined differently for each solute e.g. sodium, bicarbonate, citrate, total calcium, etc. Un-coordinated changes to citrate infusion, blood flow, CRRT fluid flow and calcium infusion flow rates can lead to "runaway" solute kinetics in terms of systemic sodium, HCO3, citrate and ionized calcium levels. In summary, the complexity of the system precludes consistent optimized prescribing by even an expert. We propose that humans should prescribe a set of clinical goals instead, e.g.: circuit iCa< 0.3mM, systemic iCa 1-1.3 mM, steady state systemic Na 140, steady state systemic HCO3 24, K=4, phosphate >= 1 mM (3.1 mg/dL), effluent dose in ml/kg/h, and patient net UF. A Web App would then generate a computationally optimized initial CVVHDF-RCA prescription based on the clinical goals, the patient's current laboratory values (systemic Na, HCO3, albumin, Hct, lactic acid, K) and patient anthropomorphic data (estimated euvolemic weight, current weight, estimated normal ECF/ICF volume + edema volume). The Web App would incorporate data on the specific CRRT machine's operational characteristics and the composition of the ACD-A citrate solution and bicarbonate based CRRT fluids (no spiking allowed) as well as the 95.2 mM CaCl2 solution prepared in D50.9NS. The Web App would use the novel fixed flow ratio CVVHDF-RCA prescribing method for highly predictable steady state solute levels. The new method of combinatorial CRRT fluid personalization without spiking would also be used. Rarely, D5W or

3% saline at a calculated rate would be used to target unusual systemic Na levels. The fidelity of the Web App versus a human prescriber achieving the same set of clinical goals at 24-hours could be easily studied.



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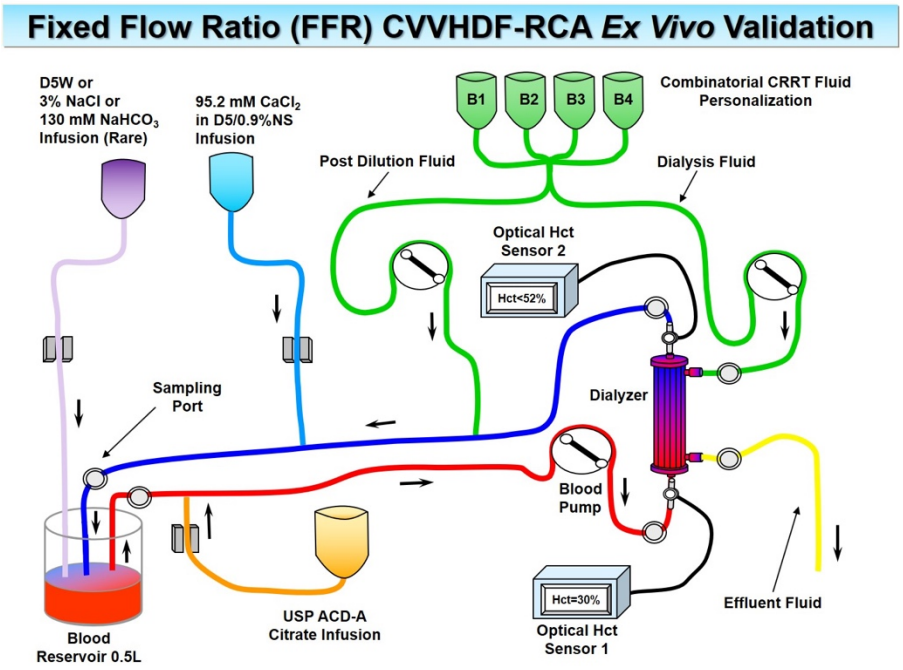
Fixed Flow Ratio (FFR) Post-Dilution CVVDF-RCA Prescribing Optimized for Simplicity and Safety

Balazs I Szamosfalvi[1], Lenar T Yessayan[1]

[1]*University of Michigan, Division of Nephrology*

Introduction: RCA is preferred for CRRT, however its use remains limited due to the complexity of most described protocols, the requirement for compounded dilute citrate solutions and the dreaded and often seemingly unpredictable complication of citrate toxicity with severe ionized hypocalcemia. We developed a novel prescribing method that maximally reduces the chance of complications and can easily be used by non-expert providers.
Body: We use a CRRT machine in post-dilution CVVHDF-RCA mode with a single 20L fluid source (scale), USP ACD-A citrate solution, only 4 types of fixed CRRT fluid compositions without spiking and 95.2 mM CaCl2 solution in D50.9NS. Crucially important that we use absolutely fixed flow ratios (FFRs): for each 1 ml/min blood flow (QB; max 150 ml/min): 3 ml/hour ACD-A flow (max rate 300 ml/h), 30 ml/h dialysate flow, 10 ml/h post-replacement flow, and about 1 ml/h Ca-infusion yielding effluent flow about 45 ml/hour (expecting some net UF) for each 1 ml/min QB. 4 CRRT fluid compositions include 140 Na, 0 or 4K, 25 or 45HCO3, 0Ca, 1 mM Mg, 0 glucose, 1.1 mM phosphate (3.4 mg/dL). By connecting 4 bags on a 20-L scale up to 25 final CRRT fluids can be combinatorically generated without spiking bags. The whole CRRT system can be ex vivo validated for targeted steady state systemic solute levels, treating a heparinized 0.5-L blood reservoir as shown in the Figure. The selected FFRs ensure >75% single pass citrate removal preventing citrate accumulation in the reservoir (despite absent metabolism). The filter (Nipro Elisio 1.5 m2) is selected carefully so that small solute dialysance is a linear function of QB up to 150 ml/min and dialysate shunting is minimized. Under these FFRs, circuit iCa is always <0.3 mM, iCa(R=reservoir) is easily maintained at 1-1.4 mM, Na(R) = Na(F=CRRT fluid) and HCO3(R) = HCO3(F)-10. We may rarely use a calculated flow of D5W or 3%saline at

a FFR to QB to target a steady state Na level up to +/-15 mM below or above 140, respectively. Example: 25 ml/kg/h x dosing weight (kg) = effluent flow ml/h. Divide this by 45 ml/h to get QB (in ml/min). Multiple QB by FFRs to get ACDA, QD, QR, and QCa (also corrected for Hct/albumin by a factor of 0.7-1.2 selected from table). Select CRRT fluids for desired K-removal and bicarbonate delivery, default is 4K, 35HCO3 (2 each of 4K/25HCO3 and 4K/45HCO3 5-L bags on 20-L scale). Effluent dose is adjusted by changing QB and all other flows with strictly FFRs all at the same time.



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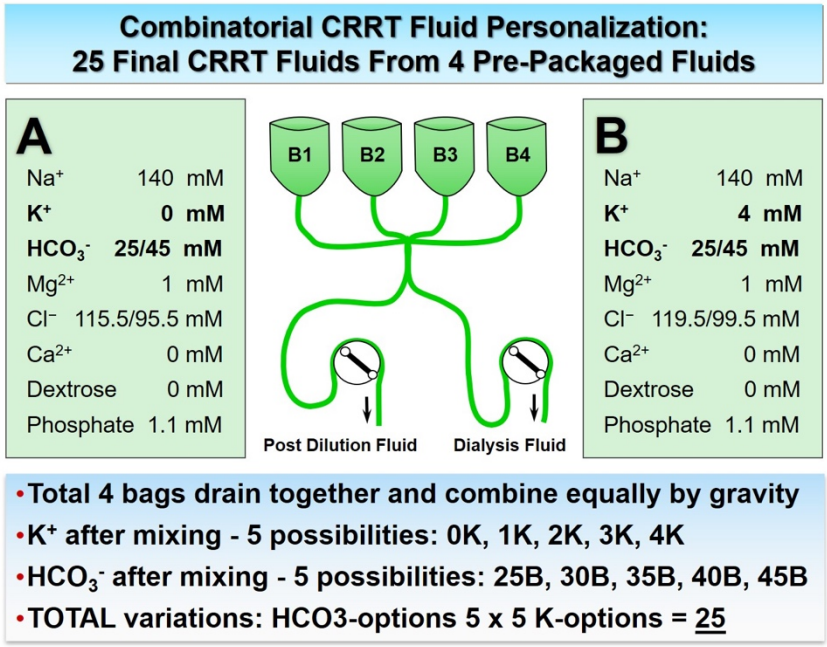
Combinatorial CRRT Fluid K and HCO3 Personalization Without Spiking Bags

Balazs I Szamosfalvi[1], Lenar T Yessayan[1]

[1]*University of Michigan, Division of Nephrology*

Introduction: In the era of sophisticated CRRT machines with integrated citrate- and Ca-pumps and (HCO3)-based Ca-free CRRT fluids, the next challenges of state-of-art CRRT-RCA delivery include the ability to provide sterile CRRT fluids customized for the patient's needs. However, in most programs customization is limited and achieved by spiking CRRT fluid bags with electrolyte concentrates or water which creates the risk of microbial contamination and human error.
Body: We developed in detail a method we call "Combinatorial CRRT Fluid Personalization" that does not require spiking of CRRT fluid bags and would allow us to use a broad range of final CRRT fluid HCO3- and K-concentrations, for which customization is most commonly needed. Many modern CRRT machines have hooks where up to 4 x 5-L CRRT fluid bags may hang at the same level and drain simultaneously by gravity at an equal rate into a common fluid line which then bifurcates (on some systems) to provide both dialysate and replacement fluid flows (see Figure). Our method would require a total of 4 types of pre-packaged fluids manufactured: 2 fluids with 0K each and either 25 or 45HCO3 (Figure, Panel A) and 2 fluids with 4K each and either 25 or 45 HCO3 (Figure, Panel B). The customized CRRT fluid will be an equal mix of 4 bags custom selected for positions B1-B4 (Figure). For each position we can either select a 0K or a 4K bag and independent

of the K-content, either a 25- or 45HCO3 bag. The final mixed fluid may have 0/1/2/3/4K level and independently 25/30/35/40/45HCO3 level for a total combinatorial fluid option count of 5 x 5 = 25 CRRT fluids from just 4-types of stock fluids. Combined with effluent flows easily adjusted with Fixed Flow Ratio (FFR) CVVHDF-RCA prescribing in the range of 1-6L/hour the final K/HCO3 fluid options should allow us to handle any clinical scenario without K or HCO3 spiking. Mg levels are optimized for CRRT-RCA. Neutral CRRT dextrose mass balance with glucose-free CRRT fluids is ensured by glucose from the ACD-A and 95.2 mM CaCl2 in D50.9NS infusions. The CRRT fluid 140 Na level will result in about 140 steady state systemic Na with FFR CVVHDF-RCA. Customization of systemic steady state Na level in the range of 125-155 mM can be achieved with infusions of D5W or 3% saline, respectively at easily calculated FFR to QB to allow us to safely treat patients with current serum Na in the range of 115 to 165 mM with the described 4-types of stock CRRT fluids without spiking.



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Monitoring of Membrane Function using Machine Pressures during Continuous Renal Replacement Therapy

Harin Rhee[1], Brendan Berenger[1], Ravindra L Mehta[1], Etienne Macedo[1]

[1]*University of California San Diego*

Purpose of the study
In operating continuous renal replacement therapy (CRRT), monitoring of filter function is an important process for the effective delivery of CRRT. Transmembrane pressure (TMP) and filter pressure drop are known to reflect membrane status, however clinical data that shows theses relations are rare.
Methods
308 filters used in CRRT at UCSD from January 1st, 2017 to December 31th, 2017 were included. All participants were treated with regional citrate anticoagulants (RCA) with calcium-containing dialysate. Underperforming filter was defined as filters changed due to clotting or low efficacy in 48 hours. Low efficacy was defined as the FUN/BUN ratio falls below 0.85. Control filter was defined as the filter that was changed

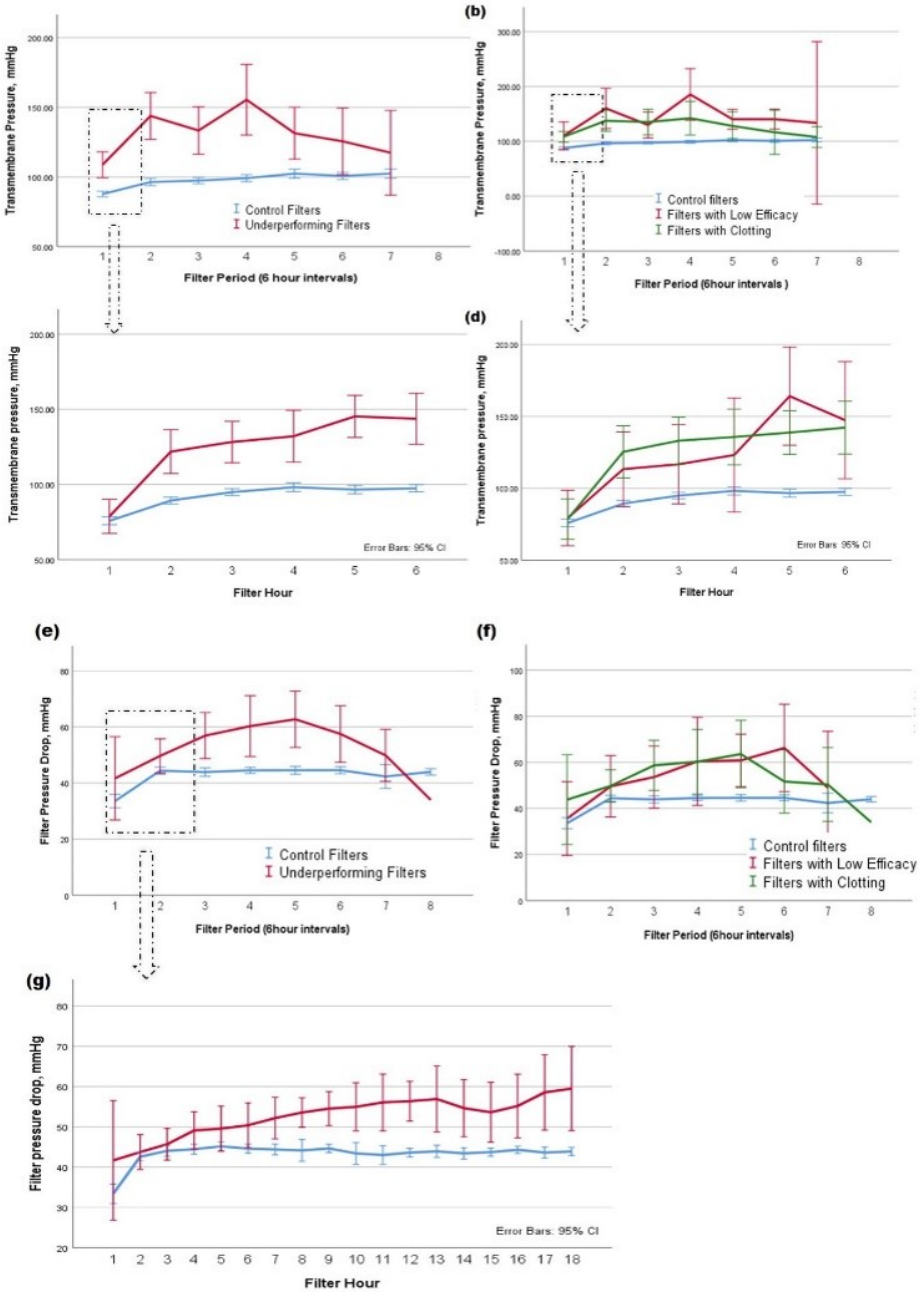
due to time limits or events non-related to the therapy. Chronological changes of TMP and filter pressure drop were compared between the underperforming and control filters.

Results

A total of 69 underperforming and 239 control filters were identified. When we compared machine pressures between the underperforming and control filters, TMP and pressure drop were significantly higher in the underperforming filters from the initial 6 hours of CRRT (Figure 1). However, there were no significant differences in machine pressures between the filters with clotting and low efficacy. In the multivariable analysis adjusted with post-filter ionized calcium and other variables, sepsis and TMP gap in the first 6 hours of CRRT were significant for the filter underperformance, and the TMP gap higher than 60.7 mmHg predicted filter underperformance with the sensitivity and specificity of 55.9 and 91.8%.

Conclusions

Both of the TMP and pressure drop reflected membrane function well and they were good markers of decreasing membrane efficacy or ongoing clotting. However, machine pressures did not discriminate clotting from low efficacy.



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Sodium Citrate 4% as an Alternative to Heparin 1,000 U/ mL for Maintaining Catheter Patency in Children

Jolyn R Morgan[1], Amanda Snyder[1], Kelli Krallman[1], Donna Claes[1], Danielle Lazear [1], Francisco Flores[1], Colleen Klosterman [1], Stuart Goldstein[1]

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Background
Central venous catheters (CVCs) are the first line of vascular access placed for children requiring renal replacement therapy or therapeutic plasma exchange (TPE). Maintaining patency when the CVC is not in use is critical in preventing premature removal. Our current strategy to maintain CVC patency involves locking both lumens with heparin 1,000 u/mL. Heparin inactivates thrombin but is associated with adverse side effects including bleeding, heparin induced antibodies, and biofilm formation. Sodium citrate 4% (SC) prevents clotting by lowering ionized calcium and is an alternative, but the potential for hypocalcemia from inadvertent flushing led to safety inquiries. We calculated a safe SC exposure using caffeine citrate, a drug used to treat apnea of prematurity and showed lower citrate exposure for SC compared to caffeine citrate even if both CVC lumens are flushed. Adult literature revealed efficacy as an anticoagulant lock and demonstrated minimal risk of bleeding, however, pediatric evidence is lacking.
Methods
We conducted a prospective crossover study assessing the efficacy and safety of locking CVCs with heparin vs. SC in children receiving HD or TPE. Patients were randomized to begin locks with SC or heparin and would crossover every 3 procedures for a maximum of 24 procedures. CVC associated blood stream infections (CLABSI) rates were hypothesized to be decreased in patients receiving SC. Secondary outcomes included Tissue Plasminogen Activator (tPA) doses required to declot CVCs, CVC replacement secondary to clotting, inability to achieve prescribed blood flow (BFR), and bleeding events. Statistical significance was assessed using chi-square analysis; a p-value of <0.05 was considered to be significant.
Results
Between June 2018 and November 2019, 17 patients were enrolled in the study HD (7) and TPE (10). A combined 178 procedures were completed with 88 (49.8%) having SC dwelling since the prior treatment. One patient in each group developed CLABSI (p=0.99). No significant difference was seen between the two groups in frequency of tPA dosing or ability to meet prescribed BFR during procedures. No CVCs required replacement and no bleeding events were observed.
Conclusion
SC is equally efficacious as heparin at maintaining CVC patency for children with similar low incidences of CVC dysfunction, bleeding, and infection rates.

	SC	Heparin	p-value
CLABSI	1 (1.1%)	1 (1.1%)	0.99
tPA Doses	6 (6.8%)	5 (5.6%)	0.73
BFR Met	81 (92.1%)	86 (95.6%)	0.33

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Pediatric CRRT: A Survey Of Program Characteristics

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Purpose of the study: Since the early reports of pediatric continuous renal replacement therapy (CRRT), the landscape has evolved over time. Recent literature suggests an increase in the frequency of the therapy, as well as better described procedures. However, there is a paucity of information on programmatic development and changes. This study's purpose is to assess the current state of individual CRRT programs as well as changes over the past decade.

Methods: Pediatric CRRT programs in the USA were provided an electronic survey, collecting de-identified programmatic level data. Participation was voluntary. Individual programs were responsible for completing the survey. Survey data was collated, analyzed and reported.

Results: 19 centers/programs completed the survey, with 11 of 19 centers (57%) providing full data. 53% programs identify themselves as critical care based nursing models and 47% as collaborative based nursing models. Yearly CRRT activity are described as low (< 10 patients), moderate (10-45 patients), and high (> 45 patients) are reported at 26%, 36%, and 38% respectively. Additionally, 4 of 19 programs report an increase in CRRT usage in the past year. 47% of programs report routine collecting quality improvement data, however the quality improvement metrics and frequency varies significantly.

Conclusion: The main findings of our study is the significant programmatic and practice variation between institutions. In spite of the significant advancements in delivering CRRT to pediatric patients, little is understood about how these variations impact patient care. Our study hopes to provide the foundation for future studies on programmatic issues such care delivery models, quality improvement, and nursing education.

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Decreasing Unplanned and Nightshift Circuit Changes for Pediatric CRRT Patients

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Introduction: Continuous renal replacement therapy (CRRT) is used in critically ill, pediatric patients with acute kidney injury and hypervolemia. Ideal circuit changes occur after 72 hours, during dayshift. Unplanned circuit changes can increase nursing workload and compromise achievement of the filtration rate goal. Additionally, circuit changes during nightshift, 1900 to 0700, can be more difficult and pose a risk to pediatric patients due to the limited number staff and resources present.

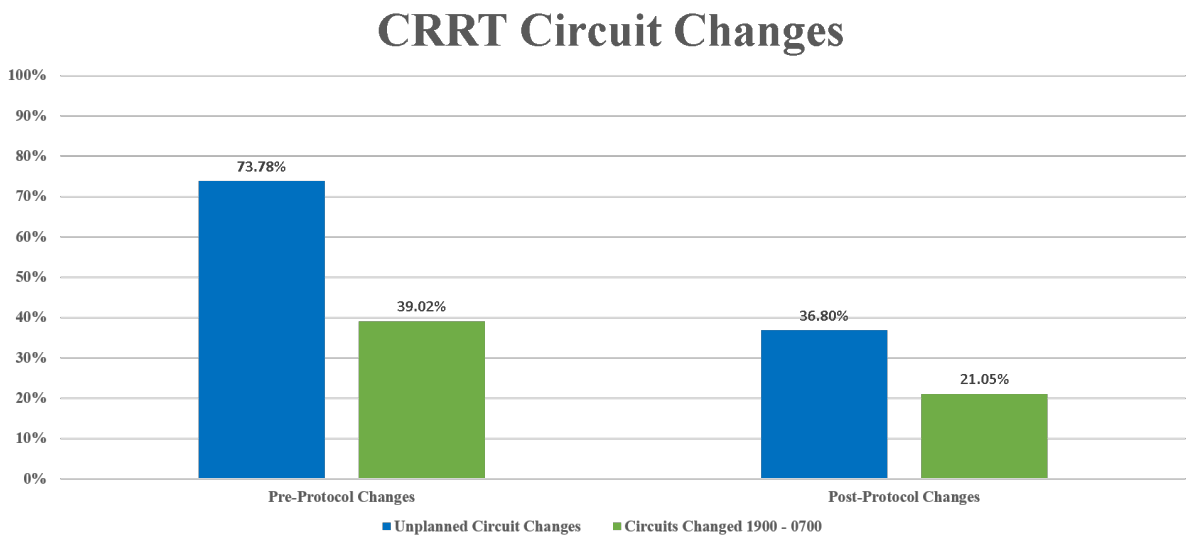
In 2015 our institution went to a nurse ran CRRT program, which includes nursing priming and initiating all

circuits. Protocol at that time, per nephrology, was to only change the circuit at the time it clotted or clogged. Due to the many challenges encountered with this protocol changes were made in the beginning of 2017. The new protocol initiated standardized circuit changes to every 72 hours, during dayshift.

Methods: A retrospective chart review of all CRRT patient circuit changes at our institution from January 2015 to December 2018 was performed. Circuit changes were divided into either planned/scheduled or unplanned, as well as whether the circuit was changed during dayshift, 0700 to 1900, or nightshift, 1900 to 0700.

Results: Following protocol changes the percentage of unplanned circuit changes decreased from 73.78% to 36.8%. Furthermore circuits changed during nightshift decreased from 39.02% to 21.05%.

Conclusion: While there are still occasions in which circuits clot or access issues occur that necessitate unplanned and/or nightshift circuit changes, the initiation of a protocol standardizing when circuit are changed has decreased the number of unplanned and nightshift circuit changes. As a result nursing workload is decreased and patient safety increased with less circuit changes occurring during nightshift.



RESEARCH II

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A Multicenter, Prospective, Randomized, Double-Blind, Placebo Controlled, Phase 2 Study to Assess the Safety & Efficacy of ANG 3777 in Patients at Risk of Developing Acute Kidney Injury after Cardiac Surgery

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Background: Acute kidney injury (AKI) is a frequent complication of cardiac surgery especially after cardiopulmonary bypass (CPB). AKI is associated with longer hospital stays, increased risk of infection, increased hospital costs, increased chronic kidney disease incidence and progression, and increased mortality. ANG-3777 (formerly BB3), a small molecule mimetic of hepatocyte growth factor, may preserve tissue viability and attenuate dysfunction in the setting of organ injury. In a previous Phase 2 study, the positive effects of ANG-3777 on urine production, serum creatinine (S Cr), and other markers of kidney function were observed in renal transplant patients.

Objectives: To describe the methodology of the GUARD (Guard Against Renal Damage) study, which aimed to evaluate the efficacy and safety of ANG-3777 in patients at risk for developing AKI following cardiac surgical procedures involving CPB.

Methods: This ongoing prospective, randomized, double-blind, placebo-controlled Phase 2 study is enrolling patients undergoing coronary artery bypass graft or heart valve repair/replacement surgery requiring CPB and at who are at elevated pre-surgery risk for AKI. Patients are randomly assigned (1:1) to received ANG-3777 (2 mg/kg) or placebo as 4 daily intravenous 30-min infusions (within 4 hours of completing CPB, 24±2 hours post-CPB, and 24±2 hours after each previous dose). Patients are being assessed for efficacy and safety up to Day 90. The primary efficacy endpoint is mean area under the curve of the percent increase in sCr above baseline over time, starting from 24 hours after end of CPB, through Day 6. Secondary efficacy endpoints include: 1) change in estimated glomerular filtration rate (eGFR) from baseline to Day 30; 2) proportion of patients diagnosed with AKI per Kidney Disease Improving Global Outcomes criteria through Day 5; and 3) length of hospitalization starting from 24 hours after end of CPB. Incidence of treatment emergent adverse events (AEs), Grade 3 or greater AEs, serious AEs, and AEs leading to discontinuation of study treatment are being recorded. Key exploratory endpoints include: 1) proportion of patients with a composite endpoint of death, ≥25% decrease in eGFR from baseline, or receiving renal replacement therapy during 30-day and 90-day post-operative periods and 2) biomarker changes of renal injury (C-reactive protein, neutrophil gelatinase associated lipocalin, kidney injury molecule-1, and S-cystatin C). Analyses of primary and secondary efficacy endpoints were based on the Full Analysis Set. Statistical tests will be 2 sided and performed at the 5% level of significance.

Conclusion: The study is ongoing in North America and Brazil. Results are expected in the second half of 2020.