ABSTRACTS

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INTERNATIONAL SOCIETY OF NEPHROLOGY
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Updates in ICU Medicine: Controversies, Challenges and Solutions

AKI & CRRT 2021

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EPIDEMIOLOGY AND OUTCOMES FROM AKI

1

The Effect in Renal Function and Vascular Decongestion in Type 1 Cardiorenal Syndrome Treated with Two Strategies of Diuretics, a Randomized Clinical Trial

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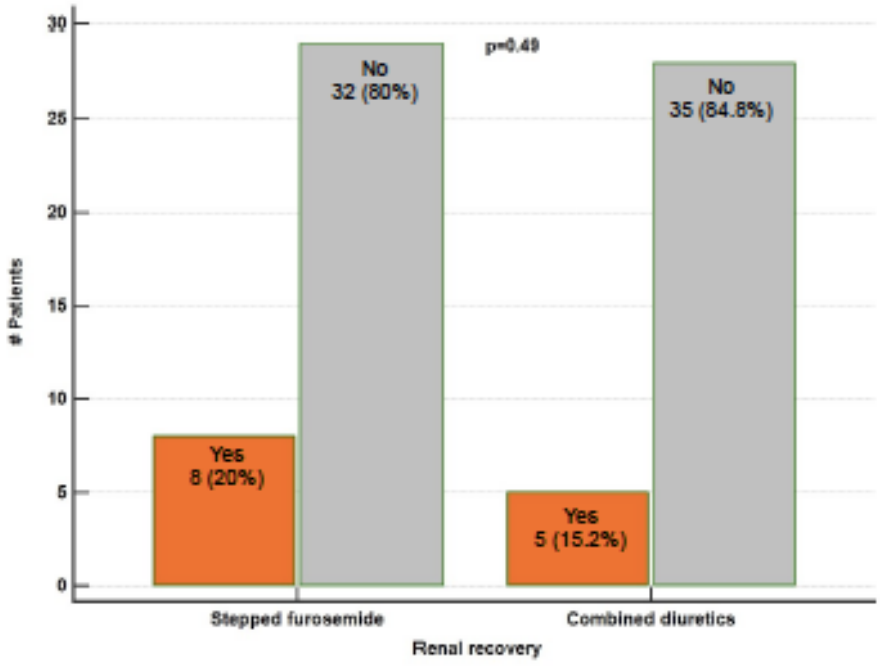
The main treatment strategy in type 1 cardiorenal syndrome (CRS1) is vascular decongestion. It is probable that sequential blockage of the renal tubule with combined
diuretics (CD) will obtain similar benefits compared with stepped-dose furosemide (SF).
Methods:
In a double-blind randomized controlled trial of CRS1 patients were allocated in a 1:1 fashion to SF or CD. The SF group received a continuous infusion of furosemide 100 mg during the first day, with daily incremental doses to 200 mg, 300 mg and 400 mg. The CD group received a combination of diuretics, including 4 consecutive days of oral
chlortalidone 50 mg, spironolactone 50 mg and infusion of furosemide 100 mg. The objectives were to assess renal function recovery and variables associated with vascular decongestion.
Results:
From July 2017 to February 2020, 80 patients were randomized, 40 to the SF and 40 to the CD group. Groups were similar at baseline and had several very high-risk features. Their mean age was 59 ± 14.5 years, there were 37 men (46.2%). The primary endpoint occurred in 20% of the SF group and 15.2% of the DC group (p= 0.49). All secondary and exploratory endpoints were similar between groups. Adverse events occurred frequently (85%) with no differences between groups (p = 0.53).
Conclusion
In patients with SCR-1 and a high risk of resistance to diuretics, the use of CD compared to SF offers the same results of renal recovery, diuresis, vascular decongestion and adverse events, and it can be considered an alternative treatment.

Figure 2. Primary endpoint Renal function recovery (*sCr return to baseline value*) in 80 patients with cardiorenal type 1 syndrome according to allocation groups.



2

AKI-IP: Development of an Interpretable Predictor for Detecting Acute Kidney Injury

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Background: Acute kidney injury (AKI) is a life-threatening condition among hospitalized patients and significantly associated with mortality and morbidity. Nearly half of AKI diagnoses in clinic were delayed, and thus early detection of AKI may

provide a crucial window for effective interventions.
Data: All patients in the open-accessed MIMIC-IV database were included. Patients with age less than 18 years, non-first ICU admission, duration of ICU stay less than or equal to 12 hours, end-stage renal disease, or developed AKI/required renal replacement therapy within the first 12 hours after ICU admission were excluded. AKI was defined according to the KDIGO criteria. Finally, a total of 35,695 patients (5,201 AKI and 30,494 non-AKI) were retrieved.
Model design: A machine learning-based Interpretable Predictor of AKI (AKI-IP) that operates sequentially hour-by-hour over individual EHR was developed. AKI-IP can output hourly probability for alerting the onset of AKI up to 12 hours in advance within the first week of ICU stay. We randomly split 85% of patients (30,339 total, 4,420 AKI and 25,919 non-AKI) for model development and 15% (5,356 total, 781 AKI and 4,575 non-AKI) for test. Forty variables from demographics, vital signs, and laboratory tests were used. In addition, A gradient-boosting-trees model of XGBoost was trained and further improved by a Bayesian optimizer and an ensemble framework. Shapley additive explanation interaction values were calculated to obtain instant interpretability, which can indicate impact of a specific feature on hourly prediction of AKI risk. Averaging the impacts across all patients shows the overall importance of the features.
Result: An area under the curve (AUC) of 0.87 was obtained when performed AKI-IP on the independent test data, which was higher than most existing models. We correctly detecting 760 AKI patients (sensitivity=0.97) while falsely identifying 1,689 non-AKI patients as AKI (specificity=0.63). The top contributed five features were differential change of SCr, SCr, ICU identifier of cardiac vascular intensive care/coronary care unit, ICU length of stay, and blood urea nitrogen.
Significance: This study focused on interpretability and real clinical application. The identified explainable risk factors can help clinicians to gain insight into how clinical variables generate quantitative influences on AKI incidents.

3

Impact of a Fluid Management Algorithm on Acute Kidney Injury in Pediatric Patients Supported on ECMO

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Introduction: Acute kidney injury (AKI) and fluid overload (FO) are associated with worse outcomes in neonatal and pediatric patients supported by extracorporeal membrane oxygenation (ECMO). We recently introduced a fluid management algorithm at our institution that included defining daily fluid balance goal with protocolized removal (diuretics and/or ultrafiltration). The purpose of this study was to evaluate the impact of this fluid algorithm on AKI incidence and survival to discharge in children supported by ECMO.

Methods: We performed a retrospective study (0 days-25years) ECMO at Children's Hospital Colorado from 2011 to 2019. Children were divided into groups based on whether or not the fluid management algorithm was used. The algorithm was implemented in 2017. The primary outcome was to assess the impact of the fluid algorithm on Kidney Disease Improving Global Outcomes (KDIGO) defined AKI that occurred after ECMO initiation. The secondary outcome was to assess the impact of any AKI (before or during ECMO), %FO and use of the algorithm on mortality. Descriptive statistics were performed to assess differences in those who were and were not treated with the fluid algorithm. Multivariable logistic regression was used to assess the associations with AKI and mortality.

Results: 299 (median age 158 days; IQR:5,1868; 45% male) children required ECMO. Veno-arterial ECMO was used in 255 (85%). AKI occurred in 58% (n=173) during the admission. AKI after ECMO initiation occurred in 38% (n=113). The fluid algorithm was applied in 74 patients. There was a significantly lower rate of AKI after ECMO initiation in those treated with the algorithm ($p<0.0001$). Cumulative %FO PreECMO and at ECMO initiation were not different between groups. Mortality was not different between groups (48% vs. 36%; $p=0.08$) (Table 1). After adjusting for confounders, utilization of the fluid algorithm was independently associated with lower odds of AKI (OR: 0.49, 95%CI: 0.27, 0.89; $p=0.02$). In the multivariable analysis, neonates compared to infants (OR 2.56, 1.22, 5.36; $p=0.01$), AKI (OR:3.12, 95%CI: 1.72, 5.66; $p=0.0002$) and FO>10% (OR:5.02, 95% CI: 2.63, 9.57;$p<0.0001$)

were independently associated with mortality.

Conclusions: Implementation of a fluid management algorithm for pediatric patients requiring ECMO was associated with decreased odds of AKI. AKI and FO>10% were associated with mortality. A multicenter prospective study is necessary to validate these findings.

Table 1: Demographics, clinical characteristics and outcomes comparing those who were and were not on the fluid algorithm

Variable	Overall (n=299)	No Fluid algorithm (n=225)	Fluid algorithm (n=74)	P value
Age (days)	158 (5, 1868)	253 (7, 2267)	39 (2, 779)	0.02
Age categories				0.04
Neonate (<30 days)	116 (39)	81 (36)	35 (47)	
Infant (30 days – 1 year)	56 (19)	39 (17)	17 (23)	
Child (>1 year)	127 (43)	105 (47)	22 (30)	
Sex (male)	140 (47)	110 (49)	44 (59.5)	0.23
Weight	5.90 (3, 17.8)	6.97 (3.1, 20)	3.67 (3, 10.8)	0.04
ECMO type				0.35
Veno-arterial	255 (85)	189 (84)	66 (89)	
Veno-venous	44 (15)	36 (16)	8 (11)	
ECMO duration (days)	5.8 (2.8, 10.7)	5.85 (2.8, 1.6)	5.63 (3.0, 10.9)	0.60
Diagnostic Category				0.04
Shock	27 (0.03)	26 (12)	1 (1)	
Respiratory	119 (40)	86 (38)	33 (45)	
Cardiac	83 (23.)	61 (27)	22 (30)	
E-CPR	70 (23)	52 (23)	18 (24)	
Any AKI (yes)	173 (58)	145 (64)	28 (38)	<0.0001
AKI Stages (any)				<0.0001
Stage 1	44 (15)	33 (15)	11 (15)	
Stage 2	35 (12)	27 (12)	8 (11)	
Stage 3	94 (31)	85 (38)	9 (12)	
Any Severe AKI	129 (43)	112 (50)	17 (23)	<0.0001
AKI Before ECMO	60 (20)	51 (23)	9 (12)	0.06
AKI on ECMO	113 (38)	94 (42)	19 (26)	0.01
Severe AKI on ECMO	79 (26)	67 (30)	12 (16)	0.02
AKI Pre-ECMO that persists on ECMO	59 (20)	50 (22)	9 (12)	0.07
RRT (yes)	36 (12)	34 (15)	2 (3)	0.003
Cumulative %FO PreECMO	9.43 (2.2, 29.7)	9,7 (2.4, 26.2)	7.6 (1.3, 36.7)	0.73
%FO>10% PreECMO	145 (49)	111 (49)	34 (46)	0.69
%FO>20% PreECMO	96 (32)	70 (31)	26 (35)	0.57
Cumulative %FO EndECMO	22.57 (7.27, 48.5)	22.2 (7.14, 49.7)	22.9 (7.9, 43.2)	0.88
%FO>10% EndECMO	206 (69)	152 (68)	54 (73)	0.47
%FO>20% EndECMO	164 (55)	121 (54)	43 (58)	0.59
Mortality	136 (46)	109 (48)	27 (36)	0.08

Continuous variables are presented as median with interquartile range, categorical variables as frequency with percent.

4

Immune Checkpoints Inhibitors-Associated Acute Kidney Injury: A Single-Centre Study

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Introduction
Immune checkpoints inhibitors (ICPi) have transformed the treatment and prognosis in some cancer types. Immune-related adverse events (irAEs) such as acute kidney injury (AKI) can occur. Our aim was to investigate the incidence, management, and outcomes of patients with ICPi-associated AKI (ICPi-AKI).
Methods
The data of all patients receiving avelumab, durvalumab, pembrolizumab, nivolumab, ipilimumab or atezolizumab in our hospital between December 2011 and November 2020 was collected. ICPi-AKI was identified as: 1) >50% increase in serum creatinine (SCr) plus either tubulointerstitial nephritis (TIN) on kidney biopsy, withholding ICPi, or steroids given due to AKI; 2) a doubling of SCr from baseline or requiring renal replacement therapy (RRT).
Results
1,170 patients were included; 190 (14.7%) patients had AKI, with 28 (2.4%) having ICPi-AKI. Of those with ICPi-AKI, 14 had underlying chronic kidney disease (CKD) and 20.7% were treated with proton-pump inhibitors prior to AKI onset. AKI stage 1 and 2 was seen in eight and twenty patients, respectively. The median time from the first and last ICPi dose to AKI onset was 104.5 (IQR 60-198) and 20 (IQR 17-34) days, respectively. Urinalysis was performed in four (14%) patients, demonstrating proteinuria in all, haematuria in 3, and leukocyturia in one patient. Renal ultrasound was performed in 18 (64%) patients and biopsy in 3 (11%) patients, all revealing TIN. Seven patients (25%) experienced concomitant extra-renal irAEs. Thirteen (46%) patients were hospitalized and one required RRT. Immunotherapy was held due to AKI in 93% of patients. 93% of patients received steroids at a median of 3 days (IQR 0-9) after AKI onset. 46% of the patients had complete renal recovery (defined as SCr 25% of baseline within 3 months from AKI diagnosis). Of note, patients whose kidney function recovered had a shorter time to steroid initiation than those with non-recovery; 0 (IQR 0-2) days vs 9 (IQR 2-23) days. ICPi was re-challenged after AKI in 6 (21%) patients; AKI recurred in 2 (33%) cases.

Conclusion
ICPi-associated AKI although rare, results in high rates of hospitalizations and treatment interruption. Our study suggests that investigations are infrequently performed in response to AKI. We suggest that greater awareness of susceptibility to AKI may limit the occurrence of these events, allow a quick response with steroid initiation and ultimately prevent the need to change the anti-cancer therapy.

5

Long-term Renal Function Outcomes in Pediatric Patients Post-CRRT

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Background and Objectives: Continuous renal replacement therapy (CRRT) is considered standard of care for management of severe acute kidney injury (AKI) in critically ill pediatric patients. There is limited data on the risk of chronic kidney disease after discharge in this pediatric patient population. We reviewed all patients who received CRRT in our intensive care units (ICU) over 5 years and assessed for development of CKD in those who survived to hospital discharge.

Design, Setting, Participants, and Measurements: This is a single-center, retrospective cohort study of all pediatric ICU patients ages 0-17 years who received CRRT from 2013-2017. The electronic health record (EHR) was used to extract demographic and clinical data. The study excluded patients with pre-existing CKD, and those who died prior to discharge or had insufficient follow-up data.

Results: Our cohort included 43 patients. Average follow-up was 29.6 months post-discharge. 32.6% (n=14) had evidence of CKD (as defined by eGFR <90 mL/min/1.73m2). A higher proportion of patients ages 0-1 years old and 12-17 years old developed CKD (p=0.04). Need for multiple courses of CRRT during admission was associated with increased risk for development of CKD (p=0.03). Both a lower baseline eGFR and lower discharge eGFR were correlated with future CKD development (p=0.009, p<0.001). An eGFR <90 mL/min/1.73m2 at discharge was

77% sensitive and 83% specific for CKD at follow-up. Only 24 patients (56%) were seen in nephrology clinic after discharge.

Conclusions: Patients who receive CRRT for acute kidney injury have a significant risk of chronic kidney disease after discharge, while follow-up in these high-risk patients with a pediatric nephrologist is sub-optimal.

Table 1: Evaluation of CKD Risk Factors in Pediatric Patients Requiring CRRT

	No CKD n=29	**CKD n=14**	**p-value**
Follow-up Time (mo), mean(SD)	33.5(18.5)	21.5 (21.1)	0.06
Age (years), mean (SD)	5.78 (4.8)	9.34 (7.8)	0.13
Sex; no (%)			0.23
- Male	13 (59.1)	9 (40.9)	
- Female	16 (76.2)	5 (23.8)	
Race; no (%)			1
- White	9 (69.2)	4 (30.8)	
- Non-white	20 (66.7)	10 (33.3)	
Primary Diagnosis; no. (%)			0.94
- Infectious/ Septic Shock	5 (83.3)	1 (16.7)	
- Cardiac	7 (70.0)	3 (30.0)	
- Heme/Onc/SCT	4 (66.7)	2 (33.3)	
- Liver/GI/Pancreas	9 (64.3)	5 (35.7)	
- Other	4 (57.1)	3 (42.9)	
Indication for CRRT; no. (%)			
- Fluid Overload	18 (62.1)	11 (37.9)	0.32
- Electrolyte Abnormalities	18 (72.0)	7 (28.0)	0.68
- Toxins	1 (100)	0 (0)	1.00
Concurrent ECMO; no. (%)			0.65
- Yes	5 (83.3)	1 (16.7)	
- No	24 (64.9)	13 (35.1)	
CRRT days mean (SD)	8.3 (9.73)	10.9 (18.9)	0.63
Courses of CRRT; no. (%)			0.03
- 1	27 (71.1)	11 (28.9)	
- 2	2 (100)	0 (0)	
- 3	0 (0)	3 (100)	

6

Integration of Severity and Duration of AKI: Impact on Outcome, A Single Center Cohort Study

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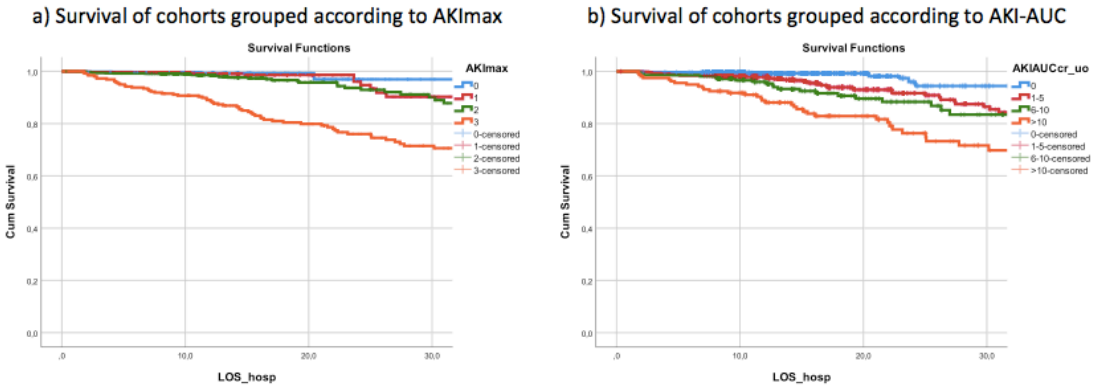
Background and goal of the study
Acute kidney injury (AKI) is a frequently occurring complication in adult patients undergoing cardiac surgery. The aim of this study is to examine the impact of AKI on survival. We evaluate the maximum severity of AKI (AKImax) according to the KDIGO classification on serum creatinine or hourly urine output, and compare this to a new approach in which we integrate AKI severity per day and duration into an area under the curve (AUC): cardiac surgery associated (CSA) AKI-AUC.
Materials and methods
Single center retrospective cohort study on patients admitted for cardiac surgery in the period 2012-2017. AKI-AUC was calculated as AKImax per day times the number of days (d); e.g. AKI stage 1 for 2 d rendered AKI-AUC = 2 and AKI stage 2 for 2 d rendered AKI-AUC = 4. We grouped AKI-AUC in 4 cohorts (0, 1-5, 6-10, >10). Correlation between data was analyzed by Pearson's Chi-square test for categoric variables and Mann-Whitney U test for continuous variables. We constructed Kaplan Meier survival curves and evaluated significance with the log-rank test. Data are reported as n (%) and median (25%-75% quartiles). Statistical significance was accepted at $p<0.05$. The local ethics committee approved this study.
Results and discussion
A total of 3469 patients were included of which 50% underwent a CABG procedure and 13% a combined CABG plus valve surgery. Patients had a median age of 70 years (61-76), 73% of patients were male and median SOFA score was 9 (7-10). AKI was observed in 63% during ICU stay, mainly stage 1 (26%) and 2 (30%). Length of hospital stay was greater in AKI patients (11.3 (9.2-17.3)) compared to non-AKI patients (9.3 (8.3-12.3)) ($p<0.001$). AKI patients had marked higher hospital mortality compared to non-AKI patients (5.7% vs. 0.9%, $p<0.001$).
We found a significant decrease in survival in patients who had AKImax stage 3, while there was no difference inbetween AKImax 1 and 2 (Figure 1a). Survival for AKI-AUC groups was lower compared to non AKI, and the AKI-AUC groups showed more differentiation on the survival curves compared to categorization on AKImax (Figure 1b).
Conclusion
In this cohort of cardiac surgery patients, integration of both severity and duration of

AKI into AKI-AUC allowed differentiation into groups with increasing severity and lower survival. This differentiation in survival curves between groups was less pronounced when they were categorized according to maximum AKI stage.



7

Acute Kidney Injury and Ethicity in COVID-19

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Background
Acute kidney injury (AKI) is a common and important complication of COVID-19 disease. However, the influence of demographics and comorbidities on AKI incidence and outcomes is not well-characterised.

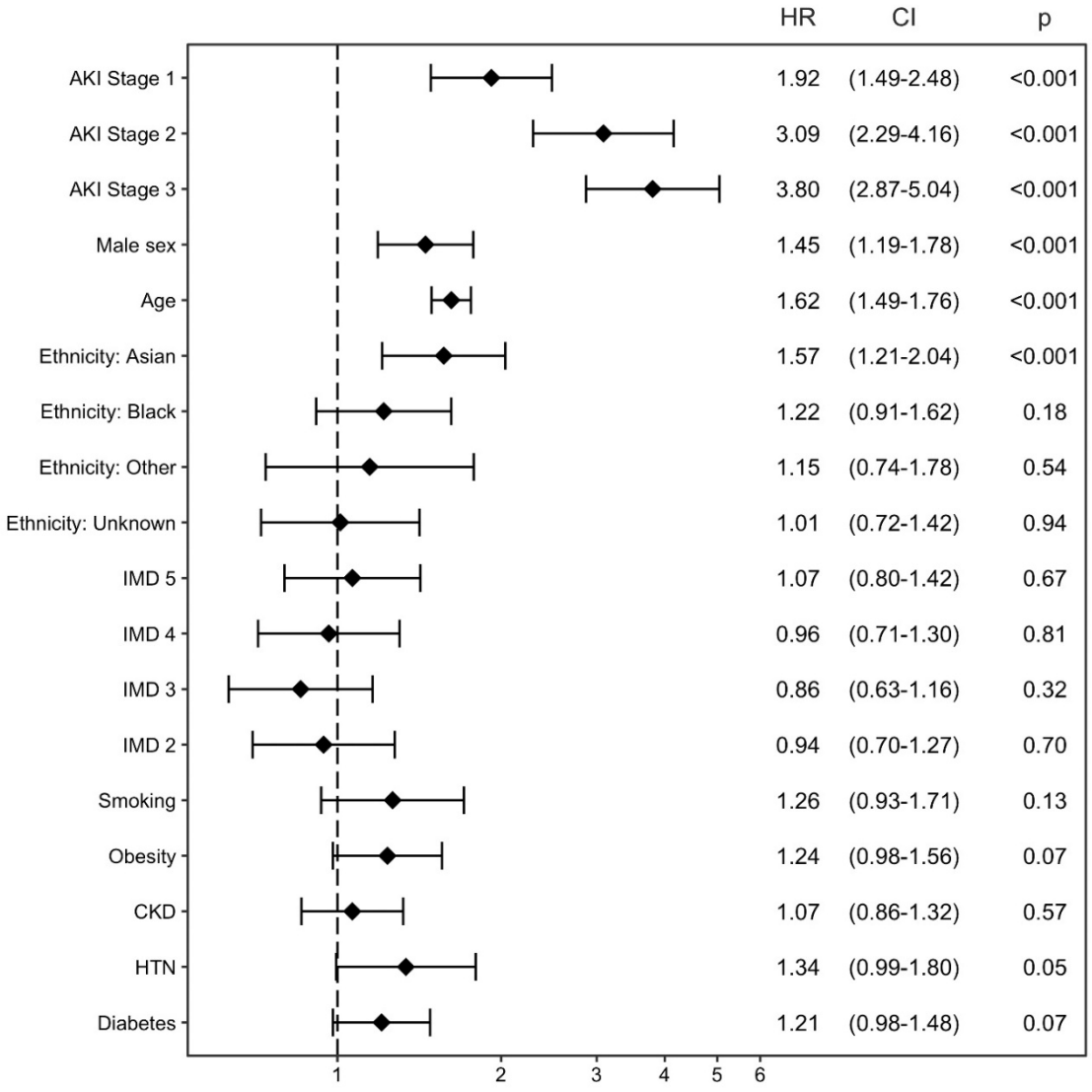
Methods
Secondary analysis of adult emergency admissions with confirmed SARS-CoV-2 infection to five London Hospitals between 1st January and 13th May 2020. Prior end

stage kidney disease was excluded. Early AKI was defined by Kidney Disease Improving Global Outcomes (KDIGO) creatinine criteria within the first 7 days after hospitalisation and sub-categorised by AKI status on and after day 7. Independent associations of AKI and survival were examined using logistic regression or Cox survival analysis, as appropriate. Results are presented as median with interquartile range, odds ratios (OR), or hazard ratios (HR) with 95% confidence intervals.

Results
Amongst 1855 COVID-19 admissions, median age was 65.0 [51.0-79.0] years, 665 (35.8%) were White ethnicity, 491 (26.5%) Asian, 299 (16.1%) Black. A total of 453 patients (24.4%) developed early AKI, 209 (46.1%) stage 1 AKI, 107 (23.6%) stage 2, and 137 (30.2%) stage 3 AKI (74 (54.0%) receiving kidney replacement therapy). Strongest associations of early AKI were male sex (OR 1.51 [1.16-1.98], p=0.002), Black ethnicity (OR 1.51 [1.05-2.17], p=0.03), diabetes (OR 1.54 [1.17-2.04], p=0.002), and secondary haemophagocytic lymphohistiocytosis score >33 (OR 2.15 [1.64-2.81], p<0.001). In patients with early AKI, 240 (53.0%) died within 30 days compared to 257 (18.3%) without early AKI. After adjustment, early AKI remained consistently associated with higher mortality: stage 1 (HR 1.92 [1.51-2.44], p <0.001), stage 2 (HR 3.01 [2.29-3.97], p<0.001), stage 3 (HR 4.08 [3.23-5.34], p<0.001. In 333 patients who developed early AKI and survived to day 7, 134 (40.2%) recovered, 47 (14.1%) recovered, but later relapsed, and 152 (45.6%) had persistent AKI at day 7, while 105 patients without early AKI developed late AKI after day 7. In survivors to day 7, persistent AKI was most strongly associated with adjusted 90-day mortality (OR 7.12 [4.30-11.87], p<0.001).

Conclusions
In an urban London COVID-19 hospital population AKI was common and strongly associated with mortality. AKI risk-factors suggest AKI could be a mediator of adverse outcomes in some high-risk groups. Trajectory of COVID-19 AKI is a key determinant of outcome.

Figure Forest plots comparing 30-day survival by stage of early AKI compared to no early AKI, results from multivariable analysis. IMD: index of multiple deprivation (1 most deprived as reference), obesity defined as BMI ≥30 kg/m^2, White ethnicity as reference, CKD: chronic kidney disease defined as baseline eGFR <60ml/min/1·72m^2, HTN: hypertension. Age modelled per 10-year increment. Age modelled per 10-year increment. Effect sizes shown as hazard ratios (HR) with 95% confidence intervals (CI). Total n=1,561, events=442.



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Outcome of Patients with Severe Leptospirosis with Acute Kidney and Lung Injury Treated with ECMO and Hemoperfusion: A Retrospective Cohort Study

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Introduction: Leptospirosis is endemic in tropical regions like in the Philippines and remains to be a public health concern. The source of infection may be direct or indirect contact with contaminated animal fluids. Annual incidence worldwide is estimated to be more than 1 million cases, including 59,000 cases of death. In the Philippines, there is an increase incidence of leptospirosis cases, with a total of 1467, 76% higher compared to the incidence of Leptospirosis in 2017 (834). Despite great efforts, there is an increasing trend of morbidity and mortality of leptospirosis. Hence, this study aimed to compare the outcome of patients with severe Leptospirosis with acute kidney and lung injury treated with extracorporeal extracorporeal membrane oxygenation (ECMO) and hemoperfusion (HP) versus those who did not receive the therapies.

Methodology: A retrospective, descriptive cohort study design was employed through review of patients with severe leptospirosis with renal and respiratory failure who received ECMO and HP versus standard therapy alone. Continuous data were analyzed using independent t test or Mann Whitney U test, and paired analysis was performed using Wilcoxon signed rank test. Categorical data were analyzed using Fisher's exact test and McNemar's test. P values ≤0.05 were considered statistically significant.

Results: Majority of the patients were males with a mean age of 35.05 ± 11.20 years old. Median mean arterial pressure (MAP) (68% vs 91.5%) and P/F ratio (91% vs 156%) were significantly higher at day 4 compared to baseline among patients who underwent ECMO and HP compared to patients who received standard therapy. Median HSCRP (134.8% vs 105.06%), procalcitonin (72% vs 18%) and SOFA score (17 [IQR: 13.5-18] vs 13 [IQR: 11-15]) were significantly lower at day 4 compared to baseline among patients who received ECMO and HP. The 28- day mortality was significantly lower in the ECMO+HP group (30%) compared to the standard therapy group (71%) (p- value= 0.013)

Conclusion: The use of ECMO and HP significantly increased the median MAP and

P/F ratio. Inflammatory markers significantly decreased on day 4 among patients who received ECMO and HP compared to patients who received standard therapy. Moreover, patients who received standard therapy have about 6 times higher odds of mortality compared to those who received ECMO+HP. Prospective or randomized clinical studies may be employed to further support the efficacy of these measures.

	n	Baseline n(%)	Day 4 n(%)	P value
MAP, median	20	68 [IQR: 56.5-81.5]	91.5 [IQR: 81.5-104.5]	0.0003
P/F ratio	20	91 [IQR: 84-105]	156 [IQR: 106.5-184.5]	0.0017
hsCRP	14	134.8 [IQR: 98.83-251]	105.06 [IQR: 32.87-124.6]	0.0057
Procalcitonin	12	72.12 [IQR: 35.92-83.74]	18.13 [IQR: 0.49-70.25]	0.0076
Inotropic requirement	20			
Norepinephrine	20	20 (100)	14 (70)	0.0143
Dopamine	20	4 (20)	1 (5)	0.0833
Dobutamine	20	1 (5)	0	0.3173
SOFA	20	17 [IQR: 13.5-18]	13 [IQR: 11-15]	0.0101
28-day mortality	20			
Yes	20	6 (30)	15 (71)	0.013
No	20	14 (70)	6 (29)	

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Management of Neonatal Acute Kidney Injury and Multiple Organ Dysfunction Syndrome in Neonatal Asphyxia: A Case Report

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Background:
Perinatal asphyxia causing multiorgan dysfunction remains a major etiology of neonatal mortality all over the world. The kidneys are one of the most affected organs

during hypoxic-ischemic (HI) events due to redistribution of cardiac output to other vital organs. The incidence rate of acute kidney injury (AKI) related to perinatal asphyxia varies from 50-70%. In a developing country where continuous kidney replacement therapy (CKRT) is unable to be delivered to neonates, acute peritoneal dialysis (PD) is the next best thing in the management of neonatal AKI related to HI event. This method is important to support the comprehensive management of other organs. We present a case of acute PD in a preterm neonate with multiorgan dysfunction related to the HI event.

Case:
A-late preterm neonate of 36 weeks' gestation presented with severe perinatal asphyxia due to placental blood flow insufficiency. He had HI encephalopathy requiring cooling therapy for 72-hours, mechanical ventilation, and inotropic support. At 36 hours of life, he developed generalized pitting edema and oliguria despite adequate fluid intake and aminophylline administration. Laboratory showed increase urea and creatinine serum, as well hyperkalemia and metabolic acidosis which support the diagnosis of acute kidney injury. Multiple organ dysfunction was also observed, involving liver, hematology, and lung. To support the fluid management, a pediatric Tenckhoff catheter was inserted by a surgeon, and manual PD was performed hourly with 10 mL/kg fill volume. Urine output was improved after 16 hours of PD initiation. PD was stopped after 9 days as normalization of urine output and improvement of kidney function. Subsequently, the improvement of other organ functions was evident.

Conclusion:
Acute peritoneal dialysis is a safe and easy method of kidney replacement therapy in the management of neonatal AKI related to HI events.

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Clinical Features and Outcomes of Acute Kidney Injury in COVID-19: A Single Centre Experience

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Acute kidney injury (AKI) is increasingly reported in COVID-19 disease and is associated with adverse outcomes. The aetiology of AKI in COVID-19 is likely to be multifactorial. This study aimed to assess the frequency and clinical features of acute kidney injury in hospitalised inpatients at a single UK centre.

Data were collected for patients admitted to University College London Hospital NHS Trust between January and June 2020 with a diagnosis of COVID-19 based on a positive SARS-CoV-2 result by polymerase chain reaction or through clinical and radiological diagnosis. Patients were categorised according to AKI stage using the KDIGO criteria. Clinical features, outcomes and laboratory parameters were reviewed.

643 patients were included for analysis. 230 developed an AKI: 45% stage 1 AKI, 21% stage 2 AKI and 33% stage 3 AKI. 52 patients required renal replacement therapy (RRT). AKI was more common in male patients, older age and patients with more comorbidities. The median time to peak AKI stage was 10 days from symptom onset; and median time to RRT was 13 days from hospital admission. 80% of patients with stage 3 AKI were admitted to ICU.

Patients with an AKI had a longer hospital admission (15 days (IQR 8 - 29 days) compared to 8 days (IQR 4 - 17 days)) and higher mortality: 51% of COVID-19 patients with an AKI died compared to 18% of COVID-19 patients without an AKI. Markers of inflammation including D-dimer, C-reactive protein and ferritin were higher in COVID-19 patients with a more severe AKI.

AKI is important to be aware of in COVID-19 patients as a marker of disease severity and a negative prognostic factor for survival. Patients with COVID-19 infection who develop an AKI have a longer inpatient length of stay and higher mortality. Early recognition and management of AKI is required in hospital inpatients with COVID-19 to reduce the progression of AKI, reduce the need for renal replacement therapy and reduce the associated mortality.

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INCIDENCE OF ACUTE KIDNEY INJURY IN A COVID-19 HOSPITAL IN THE NORTH OF MEXICO.

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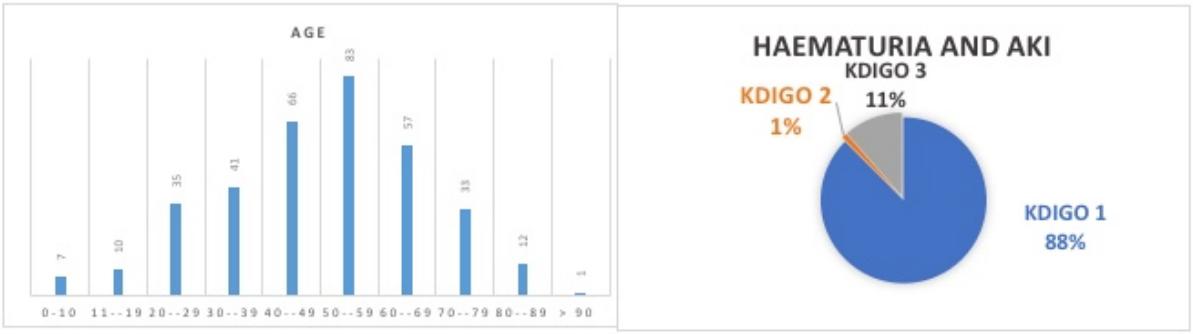
**UANL, Hospital Universitario "José Eleuterio González"*

Introduction: during 2020 the COVID-19 pandemic has brought an immeasurable burden on hospitals end medical services worldwide. One of the most frequently involved organ is the kidney (2nd place) and acute kidney injury plays a key role for increasing morbidity and mortality. The time and the risk factors for AKI development are important for optimal and effective treatment.
Methods: Retrospective, observational and descriptive study of patients from March through June 2020 were included totaling 352 patients with the diagnosis of SARS-COV-2 pneumonia with positive PCR test. The data were collected in retrospective with a submitted protocol to investigation department. No intervention was performance.
Results: Woman composed 51%. The most common age-group was 50-59 years (24%), followed by 40-49 (19%) and 60-69 (17%). The most common comorbidities were diabetes, obesity and cardiovascular disease adding up for all 30%, although 16% had 2 or more comorbidities. Upon admission 33% presented with any stage of AKD; CKD in 41/352 (12%) and AKI in 76/352 (21%). About AKI, KDIGO 1 was the most common 55%, KDIGO 2 34% and KDIGO 3 11%. From KDIGO 1 16.6% developed KDIGO 3. A total 49 patients' required Kidney replacement therapy (KRT), from these 61.2% died before discharge. 20% of the patients were under continuous replacement therapy (CRRT). From 352 patients only 163 patients had a urinalysis at hospital admission , 64.4% had proteinuria and 43.5% had haematuria. All patients with hematuria had AKI, 68% KDIGO 1 and 29% KDIGO 3. 25% of KDIGO 1 subsequently developed KDIGO 3. From all the patients without haematuria only 11% develop AKI and the majority were KDIGO 1.
Need of respiratory support (supplementary oxygen, mask, high flow Oxigen and invasive mechanical ventilation) were required for 179 patients from these 24% required mechanical ventilation and 46% of them develop AKI KDIGO 3 with KRT.
Conclusion: AKI is frequent in patients with COVID-19 pneumonia, KDIGO 1 is the most common presentation. Patients with hematuria at admission have a greater tendency to develop AKI. Patients with mechanical ventilation have greater risk to

develop KDIGO 3 and also needs kidney replacement therapy. The urialalysis could be very useful as well as the collaborative work. The absence of haematuria could be a good prognosis factor for AKI development but more data is need it.



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Urine Quinolinate To Tryptophan Ratio At Discharge And Renal Recovery At 4 Months After Community Acquired Aki: A Prospective Cohort Study

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**PGIMER, Chandigarh, INDIA*

BACKGROUND
Identifying patients at high risk of incomplete recovery from AKI is important at the time of discharge from the hospital so that they can be followed up more closely. Impaired quinolinate phosphoribosyl transferase (QPRT) activity as reflected by elevated urine quinolinate/tryptophan ratio (uQ/T) associates with the development of AKI and its recovery in prior studies. Nicotinamide supplementation is of promise as a potential intervention in this regard. We tested the hypothesis that uQ/T at hospital discharge would be higher in individuals who would show incomplete recovery at 4 months after CA-AKI (Community acquired AKI) as compared to those with complete recovery.
METHODS
The study was a prospective, observational cohort study in patients with CA-AKI who

were followed up at 1 and 4 months after discharge. Measurement of urine quinolinate and tryptophan levels at discharge was done by High-Performance Liquid Chromatography. Renal recovery at 4 months was defined as eGFR>60 ml/min/1.73 meter square and 24-hour urine protein excretion <500 mg.

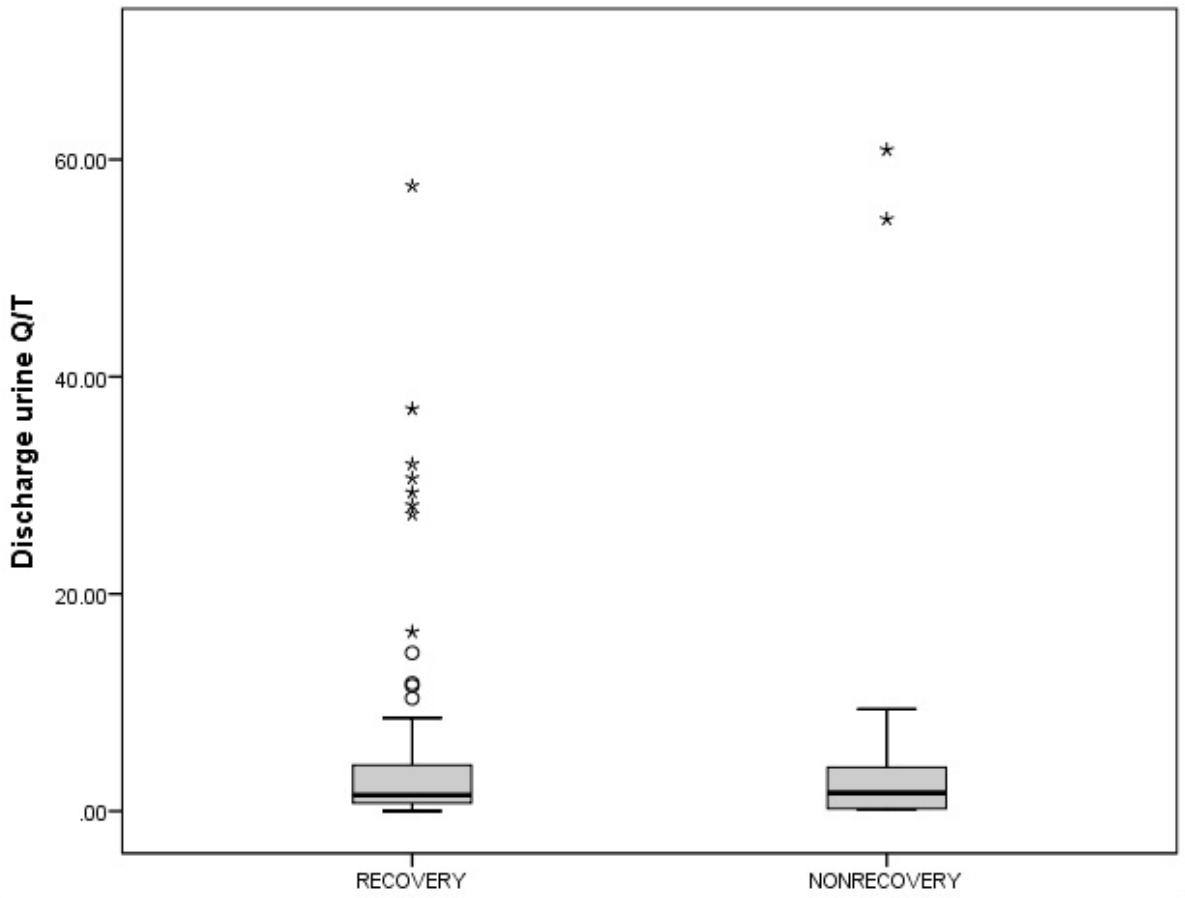
RESULTS

252 patients with CA-AKI were enrolled between February 2017 and Jan 2020. After excluding 40 patients who expired, and 84 patients who did not come for scheduled follow-ups, 128 patients were included in the present analysis. The most common causes of CA-AKI were infection (49%), obstetric (18%), toxic envenomation (11%), and drug-related (7%). The average serum creatinine in the study population at admission was 6.9±3.1 mg/dl. 95 patients received dialysis. Incomplete recovery of renal function at 4 months was observed in 29 (22.65%) out of 128 patients. As compared to the group with complete renal recovery at 4 months, age was higher, hemoglobin was lower, and hypertension was more common in the group with incomplete renal recovery. Median(IQR) urine uQ/T levels at discharge were 1.47(3.52) and 1.67(4.30) in groups with complete and incomplete renal recovery at 4 months, respectively with no statistically significant difference. (Figure 1, Table 1).

CONCLUSION

Incomplete recovery of renal function at 4 months may be seen in up to 23% of patients who are discharged from hospital after CA-AKI. Anemia, old age, and hypertension are associated with incomplete recovery. uQ/T at time of discharge from hospital in CA-AKI are not different between groups with complete versus incomplete renal recovery at 4 months. However, temporal changes in uQ/T during the course may offer more insight.

Urinary biomarkers	Recovery status	N	Median(IQR)	P value(Mann-Whitney Test)
Tryptophan (mcg/ml)	Complete recovery	92	4.82(12.96)	0.07
	Incomplete recovery	23	2.14(5.52)	
Quinolinate (mcg/ml)	Complete recovery	97	10.77(18.18)	0.40
	Incomplete recovery	25	5.32(19.23)	
Quinolinate to tryptophan (Q/T)	Complete recovery	90	1.47(3.52)	0.75
	Incomplete recovery	23	1.67(4.3)	



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Weekend Effect on the Incidence and Prognosis of Cardiac Surgery Associated-Acute Kidney Injury

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Objective: Whether surgery time affects the occurrence and prognosis of cardiac surgery associated-acute kidney injury (CSA-AKI) remains unclear. 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. The primary endpoints were the incidences of CSA-AKI and AKI requiring renal placement therapy (AKI-RRT). The secondary endpoints included hospitalization time, length of intensive care unit (ICU) stay, mechanical ventilation time, incidence of short-term adverse events after surgery (including death and treatment abandonment), hospitalization costs, and renal recovery.
Results: A total of 1974 patients aged from 18 to 80 were enrolled. 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). The incidence of severe AKI and AKI-RRT showed no significant difference between the two groups. The length of hospitalization for AKI patients in the weekend group was significantly shorter than that in workdays (13 [10, 17] days vs. 14 [11, 19] days, P= 0.011). However, no statistical difference was found between weekend group and workday group in terms of other short-term endpoints. Multivariate logistic regression analysis revealed that weekend surgery was among independent risk factors of CSA-AKI.
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.

	Workday group (N=1808)	Weekend group (N=166)	P value
AKI incidence [n(%)]	628(34.7%)	71(42.8%)	0.038
Initial AKI stage			0.509
- Stage 1	518(28.7%)	58(34.9%)	
- Stage 2	52(2.9%)	4(2.4%)	
- Stage 3	58(3.2%)	9(5.4%)	
AKI progression [n(%)]	134(21.4%)	13(18.6%)	0.588
Severe AKI [n(%)]	141(7.8%)	18 (10.8%)	0.167
AKI-RRT [n(%)]	80(4.4%)	9(5.4%)	0.554
Duration between RRT and surgery (d)	1[1,4]	2[1,2.5]	0.972
Urine output at RRT initiation (ml)	610[215, 1213]	610[160, 1475]	0.866
RRT sessions (n)	4[2,6]	1[1,7]	0.137

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Evaluation of a UK Multi NHS Trust Acute Kidney Injury Quality Improvement Patient Safety Collaborative

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Acute Kidney Injury (AKI) is a common complication affecting one in five hospital emergency admissions in the UK. In 2015, an AKI patient safety quality improvement collaborative (QIC) was established by an organisation named UCLPartners with nine participating UK NHS Trusts, to help improve AKI measures of care and reduce AKI mortality. Improvements in AKI care were evaluated using the Institute for Improvement Breakthrough Series (IHI BTS), which encourages shared learning from organisations to facilitate improvement. Members of all trusts met regularly over 22 months to discuss improvements, implement these using Plan-Do-Study-Act cycles and share their learning through storyboards. Monthly data on pre-selected outcome and process measures was collected and returned to UCLP for trust level collaborative analysis. In return, UCLP facilitated learning sessions, measurement days and regular quality improvement training as well as open media collaborative resources.

Four of the nine hospitals provided consistent data over the 22 collection points, with 1029 AKI episodes evaluated in total. Data from the first six months was compared with data from the final six. Overall, process measures improved with the median recognition of AKI within four hours of a hospital admission increasing from 72% to 95% (P=0.04). The median percentage of treatments given on time to patients with an AKI increased by 24%, to 92% overall (P=0.002).In terms of outcome measures, AKI mortality showed the most successful results with the median AKI 30 day mortality decreasing from 30% to 16%, a reduction of 47% (P=0.05). Renal function recovery at 30 days following hospital admission also improved over the course of the collaborative by 19.5% to 75% (P=0.008).

The results demonstrate a sustained improvement in the care received by inpatients with AKI. Furthermore a positive shift in workplace culture was noted, including growth of interconnected networks and improved inter-departmental communication. Key challenges included difficulties in consistent engagement of stakeholders due to competing clinical and non-clinical priorities, the importance of senior management

support and the pitfalls of reliable data collection due to limited human and technical resources. Most of these challenges can be overcome through increased resource provision, identifying essential stakeholders from the outset, and early involvement of senior executives to help make collaboratives even more successful.

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CENTRE VARIATION IN MORTALITY FOLLOWING HOSPITAL-ACQUIRED ACUTE KIDNEY INJURY: Analysis of a large national cohort

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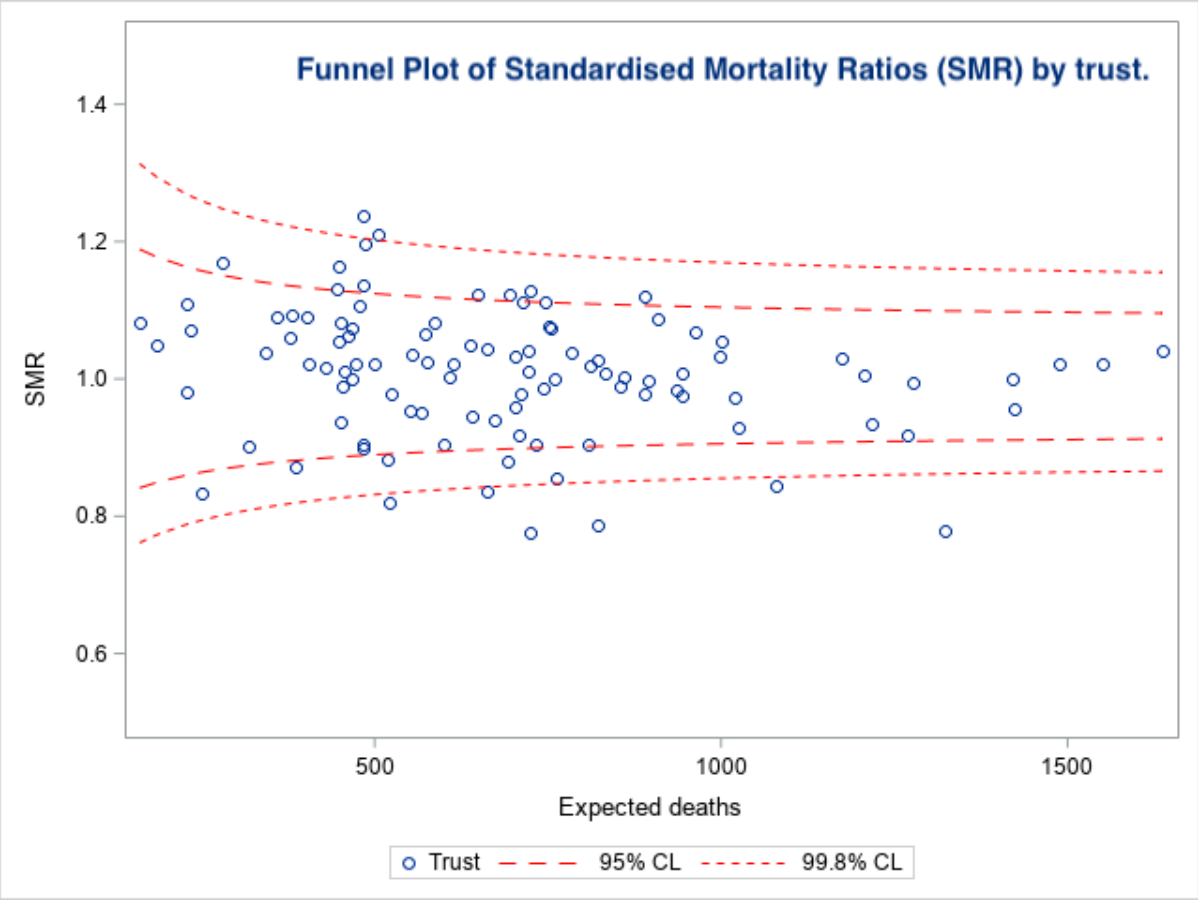
Background: Monitoring of outcomes for patients with Acute Kidney Injury(AKI) is necessary to drive quality improvement in AKI care. In this study we describe development of a case-mix adjusted 30-day mortality indicator for patients with hospital-acquired AKI(HA-AKI), to facilitate identification of unwarranted variation in outcomes across hospitals in England.

Methods: We utilised a routinely collected national dataset of biochemically defined AKI cases, linked with hospitals administrative and mortality data. 250,504 HA-AKI episodes were studied across 103 hospitals between January 2017 - December 2018. Standardised mortality ratios were calculated for each hospital using logistic regression; adjusting for age, sex, primary diagnosis, comorbidity score, AKI severity, month of AKI, and admission method.

Results: Mean 30-day mortality rate was high at 28.6% and varied considerably between hospitals (22.3%-35.5%), with 23/103 classed as outliers(95% control limits) - (Figure 1_. Patients with HA-AKI had mortality rates more than 5 times higher than the overall hospitalized population in 90/136 diagnosis groups and over 10 times higher in 60/136 groups. Presentation at hospitals with on-site nephrology services

was associated with lower mortality risk, as was Asian or Black ethnicity. Deprivation however was associated with higher risk of death.

Conclusions: This is the largest multi-centre analysis of mortality for patients with biochemically ascertained HA-AKI to date, once again highlighting AKI as an important patient safety concern across hospital settings. Centres identified as having poor outcomes will need to carefully interrogate their AKI care pathways to understand and address reasons for this, with national strategies required to tackle identified health inequalities.



Pre and Postoperative Neutrophil-to-Platelet*Lymphocyte Ratio as predictors of Early Postoperative Acute Kidney Injury Following cardiovascular surgery

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Background：Acute kidney injury (AKI) is a common and serious complications after cardiovascular surgery. According to previous research, postoperative low platelet count and perioperative high neutrophil/lymphocyte (N/L) ratio were reported as predictors for a cardiovascular surgery associated with AKI (CSA-AKI) and mortality. In this study, we aimed to investigate the prognostic significance of the combination neutrophil/lymphocyte*platelet ratio (NLPR) at the time of admission to hospital and intensive unit (ICU) in predicting CSA-AKI.
Methods：We prospectively studied 2449 adult patients who underwent cardiovascular surgery during July 2019 to December 2019. The preoperative, intraoperative, and postoperative variables of these patients were collected. NLPR was determined using neurtrophil counts, lymphocyte and platelet counts at the two time points (admission to hospital and ICU). Dose-response relationship analysis were applied to quantify the risk of CSA-AKI along with the NLPR levels. Predictive ability of NLPR was estimated through the area under the receiver operating characteristic (AUROC) curves.
Results: Totally 838 (34.2%) patients developed CSA-AKI with stage 1 (n=658, 26.8%), stage 2 (n=131, 5.4%) and stage 3(n=49, 2.0%). The indicators of NLPR during perioperative period were associated with increased AKI risk. However, the effect of NLPR on AKI was not of a simple linear relation, but a “J” shape nonlinear relation. In the restricted cubic spline models, the risk of CSA-AKI was relatively flat until 1.0 of preoperative NLPR and increased rapidly afterwards, with an odds ratio of 1.13 (1.06 to 1.19) per 1 unit. Similarly, patients whose postoperative NLPR value were >10 were more likely to develop AKI with an OR of 1.02 for every 1 unit increase. Integrating the dynamic NLPRs into multiple predictive model, we found that the AUC was up to 0.798 (95% CI 0.786~0.812).

Conclusion: The perioperative increased level of NPLR which can be calculated by simple method from routine blood analysis showed us that this parameter is independent biomarker directly related to development of acute kidney injury during the perioperative period.

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Urinary Biomarkers and Major Adverse Kidney Events (MAKE) in Patients with COVID-19

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**Instituto Nacional de Enfermedades Respiratorias*

SARS-Cov2 is a new RNA virus responsable of the COVID-19 pandemic. Some serum inflammatory biomarkers, such as ferritin, D-dimer (DD), C reactive protein (CRP), Creatine phosphokinase (CPK) and lymphocyte count are associated with worse outcomes.
Acute kidney injury is a common complication that increases mortality in epidemiological studies. Since SARS COV2 has mostly been found in tubules, we wondered if urinary biomarkers could predict MAKE earlier than risk factors already identified so far.
The aim of this study was to compare urinary biomarkers levels between the MAKE and no-MAKE group.(MAKE= acute kidney injury, renal replacement therapy, death and loss of >25% of GFR after discharge) in patients with COVID-19 hospitalized at the Instituto Nacional de Enfermedades Respiratorias (INER).
Methods: Prospective cohort study. We included 51 individuals with severe pneumonia caused by SARS-CoV2, confirmed by RT-PCR, from May to August 2020. We included patients >18 years old; with no history of chronic kidney disease; and PaO2/FiO2< 300 mmHg on admission. They were followed until discharge. Demographics, comorbidities, clinical and laboratory data were recorded.
We collected fresh urine from recruited patients in the first 5 days upon arrival. A second sample was collected 5 days later as follow up. Urine samples were immediately frozen at -80ºC until processing. Neutrophil gelatinase associated lipocalin (NGAL), urinary tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP-7) were measured in every urine sample with an ELISA kit. The platform Architect® (Abbott) was used for N-Gal.
Statistical analysis: Data was expressed as means and standard deviations(SD) or medians and interquartile ranges and proportions for categorical variables. Mann Whitney U test was used to compared measurements between groups.
Results: Statistical significant differences were found in NGAL, IGFBP7 and

TIMP2/IGFBP7 at baseline while between inflammatory serum markers, BUN, DD and CPK differences were statistically significant. At day 5 NGAL, IGFBP-7 and TIMP2/IGFBP-7 were statistically different and so were CPK, DD and BUN. Conclusion: Urinary biomarkers levels were different between MAKE and no MAKE patients. They could potentially be useful to predict the composite outcome. Serum inflammatory biomarkers were also different between the analysed groups, reinforcing what has been published before in other populations.

		No-MAKE	MAKE	p value
URINARY BIOMARKERS				
Urine NGAL (ng/ml)	Baseline	32.40 (20.20-44.50)	36.40 (34.40-329.20)	**.010**
	Day 5	34.85 (10-59.70)	32.70 (17.70-49.30)	**.008**
IGFBP-7 (ng/ml)	Baseline	10.01(9.84-17.62)	14.26 (12.78-22.05)	**.050**
	Day 5	18.82(15.52-22.12)	14.99 (12.20-23.85)	**.013**
TIMP-2 (ng/ml)	Baseline	5.50 (5.04-5.96)	3.04 (3.02-6.50)	.063
	Day 5	3.43 (3.15-3.71)	5.41 (3.82-7.36)	.419
(TIMP-2/IGFBP-7)/1000	Baseline	0.58 (0.05-0.08)	.083 (0.67-0.27)	**.007**
	Day 5	0.09 (0.085-0.19)	0.15 (0.16-0.61)	.225
BLOOD AND SERUM INFLAMATORY MARKERS				
Hemoglobin (g/dL)	Baseline	10.5 (9.5-12)	13.1 (13-13.5)	.856
	Day 5	13.35 (11.5-15.2)	13.9 (11.1-14.2)	.723
Leucocytes (10^3/mm3)	Baseline	5.0 (3.9-6.4)	6.85 (5.8-9.3)	.159
	Day 5	7 (6.9-7.1)	9.8 (9.1-10.3)	**.010**
Lymphocites (10^3/mm3)	Baseline	0.5 (0.4-1.0)	0.3 (0.2-0.5)	.198
	Day 5	0.8 (0.4-1.2)	0.6 (0.4-1.0)	**.007**
Platelets (10^3/mm3)	Baseline	212 (206-276)	193 (188-280)	.433
	Day 5	404 (346-462)	308 (275-371)	.079
BUN (g/dL)	baseline	9.5 (6-16)	21 (17-39)	**.000**
	Day 5	17.5 (14.0-21.0)	45 (28-58)	**.000**
LDH (UI/L)	Baseline	213 (196-413)	293 (290-317)	.863
	Day 5	292 (254-331)	287 (250-344)	**.021**
CPK (UI/L)	Baseline	25 (13-39)	22.5 (22-31)	**.007**
	Day 5	45.5 (27-64)	298 (99-707)	**.002**
D Dimer (ug/mL)	Baseline	0.34 (0.31—0.46)	0.72 (0.44-1.28)	**.012**
	Day 5	1.07 (0.16-1.99)	4.9 (1.3-3.58)	**.000**
C-Reactive Protein (mg/dL)	Baseline	3.77 (1.4-13.66)	10.0 (8.2-12.3)	.082
	Day 5	2.12 (1.11-3.13)	4.9 (1.3-15.5)	**.002**
Fibrinogen (mg/dl)	Baseline	545 (535-587)	560 (533-752)	.702
	Day 5			
Procalcitonin	Baseline	0.14 (0.08-0.18)	0.42 (0.15-0.75)	.127
	Day 5	0.10 (0.07-0.13)	0.14 (0.070.42)	**.016**
Troponin (pg/mL)	Baseline	7.2 (4.6-8.4)	14.4 (3.3-39.4)	.128
	Day 5	19.0 (0.0-38)	10.5 (4.6-14.0)	**.002**
Ferritin (ng/mL)	Baseline	675.9 (418-953)	2472 (2424-2515)	.788
	Day 5	733 (715-751)	1202 (745-1362)	**.016**

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Continues renal replacement therapy in Acute kidney injury after liver transplantation in National cancer center in Mongolia

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**National cancer center Mongolia*

Continues renal replacement therapy in Acute kidney injury after liver transplantation in National cancer center in Mongolia
Introduction:
Liver transplantation has become a widely accepted treatment for a variety of liver diseases, such as viral and alcoholic cirrhosis, liver malignancy, acute liver failure, and many metabolic abnormalities. Most common complication is Acute kidney injury. Post-operative care of liver transplantation, condition of the patient and hemodynamic has to be monitored at ICU until these are improved.
Method:
We have performed 21 LT in NCCM /13 male, 8 female/ in our hospital. 17 cases on LDLT, 4 cases are DDLT. After liver transplantation, 7 patients have acute kidney injury, we used CRRT 3 trouble condition patient.
Since September 2019, 3/21 (14.2%) patients entered in the CRRT. The primary reasons for the initiation of continuous renal replacement therapy (CRRT) were treatment of fluid overload and electrolyte imbalance , acidosis, and anuria.
Result:
3 patients are (100%) survived now. For example: The patient, 44 years old, male diagnosed with HCC in liver with cirrhosis, with portal hypertention, ascites, and hepatorenal syndrome. Pre surgical Lab investigation: Lab: Blood test: WBC-4.5, RBC-3,8 HGB-13.1, HCT-38.3, PLT-53 Biochemistry: Alibumin-30.0, BUN-13.8, T protein-55.3, ALAT-62.8, ASAT-89.5, T Bilirubin-46, Cretinin-217.2, Na-141, K-4.2. Living donor liver transplantation was successfully done. The operation time was 9 hours. Blood loss was 400ml, intraoperative fluid was transfused blood 490, plasma solution 11000, urine output is 600ml. vasopressin nor, When admitted to the ICU intubated, after operation laboratory experiments are increased, BUN 24mmol/l, creatinine 333mmol/l, hyperkalemia 6.9mmol/l, pulmonary and all body edema, urine output is decreased. We connected CRRT 28hours, ultrafiltrated 100ml/h. After CRRT patient condition and laboratory experiments are increased, creatinine and bun are measured normal range, no edema.
Conclusion:

We performed CRRT in NCC, first time. Although CRRT may provide some benefits for people with acute kidney injury, CRRT effectiveness for acute kidney injury.

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Acute Kidney Injury in Critically Ill Children Associated with SARS-CoV2 Infection (Global Pediatric Assessment of the First Three Months of COVID Pandemic)

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Purpose: Adult patients infected by the novel SARS-CoV2 virus demonstrate a high prevalence of AKI (acute kidney injury), including severe AKI. Children exposed to the virus appear to be at high-risk for multiorgan dysfunction as adult patients; however, the epidemiology and risk factors for AKI in children exposed to the SARS-CoV2 virus are unknown.
Methods: We conducted a sequential point-prevalence international study across 42 centers to assess the epidemiology of AKI in critically ill children suspected of exposure to the SARS-CoV2 virus. Data were captured once weekly over 12-consecutive weeks between April and June of 2020. Patients under investigation (PUI) were followed to determine infection exposure, AKI stage (KDIGO creatinine-based staging), resource utilization, and patient outcome. Positive patients (CONFIRMED) were determined by either polymerase chain reaction positivity or antibody positivity. AKI was determined in the first 14 days. If unavailable, baseline creatinine was estimated using eGFR assumed to be 120 ml/min/1.73m2.
Results: In 331 PUI children (male 185, 55.9%, age 11 years (3,16)), 179 (54.1%) were CONFIRMED, and 124 (37.5%) had AKI. In these patients, 78 (23.6%) required vasoactives, 83 (25.1%) required invasive ventilation, 6 (1.8%) extracorporeal membrane oxygenation, 4 (1.2%) required renal replacement therapy, and 14 (4.2%) died.

Amongst the CONFIRMED patients, 74 (41.3%) had AKI, 35 (19.6%) had severe AKI. Of the CONFIRMED-AKI cohort (74), 25 (69.4%) required vasoactives, 26 (73.3%) required invasive ventilation, and 7 (20%) died. Univariate effect estimates identified shock and respiratory support to be associated with increased risk of AKI but these did not carry significance in multivariate analysis.
Conclusions: AKI and severe AKI demonstrate a high prevalence in critically ill children suspected of having SARS-CoV2. AKI prevalence is more common in these patients than in existing global epidemiologic observational studies of children requiring intensive care (41.3% vs. 26.7% for all AKI and 19.6% vs. 11.2% for severe AKI). In this global study, AKI in pediatric SARS-CoV2 patients is similar to rates seen in adult patients (44-50% in reported data) but disease related severity appears reduced (mortality, extracorporeal therapy, kidney support therapy use). A comprehensive analysis of pediatric patients is underway and is needed to characterize the unique aspects of AKI in these patients.

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Clinical Course and Outcomes of AKI Requiring RRT in SARS-CoV-2 ARDS: A Single-Center Retrospective Observational Study

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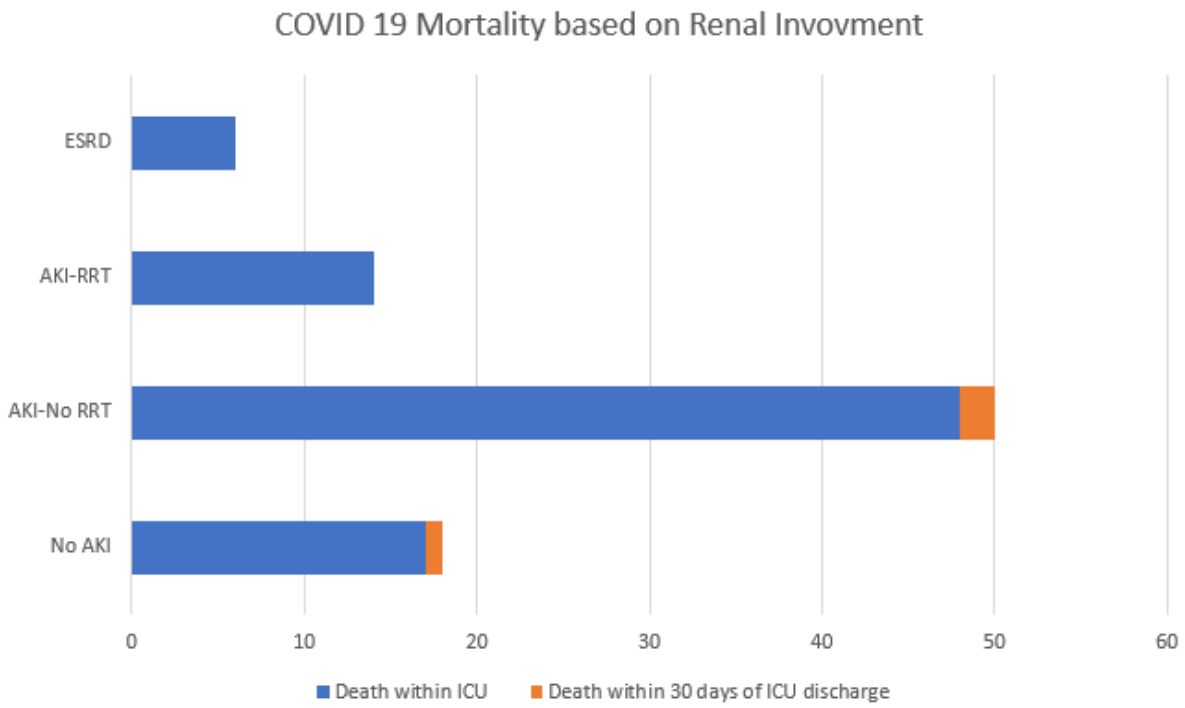
Purpose:The recent pandemic of SARS-CoV-2 has challenged healthcare systems worldwide in their ability to care for high volumes of critically ill individuals. Acute kidney injury (AKI) is a known serious complication of critical illness, associated with increased mortality, resource utilization and healthcare costs. Reported outcomes of COVID-19 critical illness and associated AKI are highly variable, and confounded by strain on the healthcare system, availability of resources and initiation strategies of renal replacement therapy (RRT). We sought to investigate the outcomes of AKI-RRT, in comparison to ESRD, AKI without need for RRT and absence of AKI in the context of severe COVID-19 infection requiring ICU admission at our institution.
Methods and Design: We performed a single-center retrospective analysis of all patients with severe COVID-19 infection, admitted to ICU level of care at Brigham

and Women's Hospital between 3/1 and 6/1/2020. We stratified patients into four cohorts (no AKI, AKI not requiring RRT, AKI-RRT and preexisting ESRD), and we investigated comprehensive demographic, clinical and laboratory data. Results: We identified 272 patients with acute COVID-19 infection admitted to one of the BWH ICUs between 3/1 and 6/1/2020. 19 patients had reasons for ICU admission unrelated to coincident COVID-19 PCR positivity and were excluded from further study. From the 253 patients analyzed, 105 did not have AKI, 100 had AKI not requiring RRT, 36 had AKI-RRT, and 12 had preexisting ESRD. Mortality on ICU or within 30 days of ICU admission was 18/105 (17.1%) for no AKI, 50/100 (50%) for AKI/no RRT, 14/36 (38.9%) for AKI-RRT and 6/12 (50%) for ESRD. AKI and AKI-RRT were associated with prolonged ICU admissions, higher ICU readmission rates, and worse respiratory and hemodynamic parameters. RRT was predominantly initiated for volume management. From 36 patient initiated on RRT, RRT was successfully discontinued in 23 cases, of which 2 died in the later course. Conclusions:In a resource-rich environment with no limitations to ICU capacity and RRT availability, COVID-19-related AKI is a marker of critical illness severity, coinciding with worse cardiopulmonary morbidity and mortality. We did not observe any mortality specifically attributed to AKI or RRT-related complications. Survivors of COVID-19 critical illness demonstrate an excellent prognosis of AKI recovery, with high rates of successful RRT discontinuation and rare persistence of advanced CKD.



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Annexin A1 tripeptide mimetic increases sirtuin-3 to augment mitochondrial function and limit ischemic kidney injury

Hagir Suliman*, Qing Ma*, Zhiquan Zhang*, Jiafa Ren*, Benjamin T Morris*, Steven D Crowley*, Luis Ulloa*, Jamie R Privratsky*

**Duke University*

Rationale: Acute kidney injury (AKI) is one of the most common organ failures following surgery. The potential exists to give therapies prior to known kidney insult to limit AKI; however, specific kidney protective therapeutics are lacking. We have developed a tripeptide mimetic (ANXA1sp) derived from the N-terminal domain of the parent annexin A1 molecule that shows promise as an organ protectant limiting cellular stress; however, its potential as a kidney protective agent remains unexplored, and its mechanism of action is poorly understood. Our hypothesis was that ANXA1sp would limit kidney injury and improve mitochondrial function following surgical ischemic kidney injury.

Methods: In blinded fashion, wildtype mice were assigned to receive vehicle control or experimental drug (ANXA1sp) 1 hour prior to and 1 hour after kidney vascular clamping, and daily thereafter until sacrifice. Kidney injury and function were assessed by measurement of serum creatinine and blood urea nitrogen (BUN) and histologic injury scoring of kidney tissue sections. Cell death and oxidative stress in kidney tissue sections were measured by immunofluorescence microscopy. Real-time PCR and western blot were used to assess sirtuin-3 (SIRT3) levels and mitochondrial health via markers associated with mitochondrial fragmentation, mitophagy, and mitochondrial biogenesis. The necessity of SIRT3 to ANXA1sp-mediated kidney mitochondrial protection was assessed by an in vitro model of oxygen-glucose deprivation in immortalized kidney tubule cells.

Results: ANXA1sp ameliorated severe ischemic AKI (Fig. 1a) and hastened return of kidney function following moderate ischemic AKI (Fig. 1b). ANXA1sp limited kidney cell death and oxidative stress following ischemia. ANXA1sp upregulated

markers associated with improved mitochondrial DNA transcription, mitochondrial biogenesis, and removal of damaged mitochondria. ANXA1sp upregulated expression of the mitochondrial protectant SIRT3 in the mitochondria of kidney tubular cells. Silencing of SIRT3 limited ANXA1sp-mediated protection against hypoxic cell death.

Conclusions: ANXA1sp limits kidney injury through upregulation of SIRT3 and consequent preservation of mitochondrial function. Due to the extensive contributions of mitochondria to cellular metabolism and survival, ANXA1sp holds considerable promise as a perioperative kidney protectant.

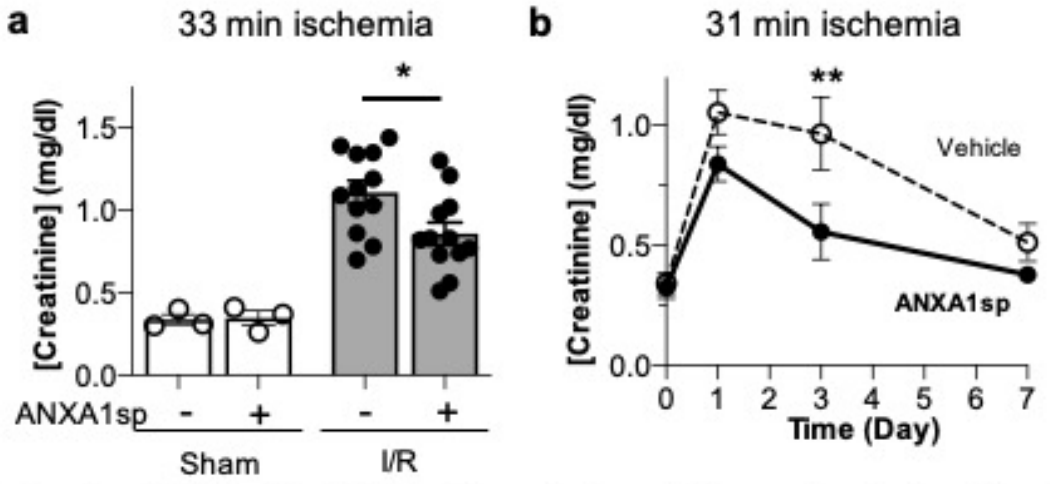

Fig. 1 – AnnexinA1 tripeptide (ANXA1sp) given prior to and after vascular clamping attenuates (a) severe ischemic AKI and (b) hastens return of kidney function following moderate ischemic AKI. Graphs display mean +/- SEM. Statistical significance determined by two-way ANOVA (*p=0.05, **p<0.01).

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Nephrologist interventions to avoid kidney replacement therapy in acute kidney injury

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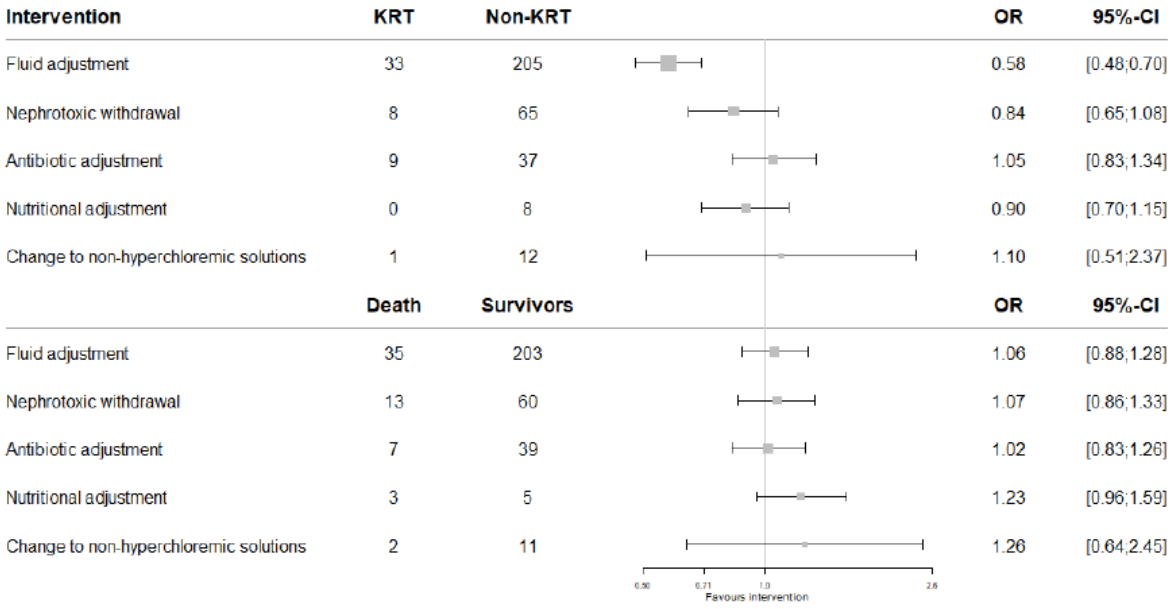
Background: Based on the pathophysiology of acute kidney injury (AKI) it is plausible that certain early interventions by the nephrologist could influence its trajectory. In this study, we investigated the impact of 5 early nephrology interventions on starting kidney replacement therapy (KRT), AKI progression and death.
Methods
In a prospective cohort at Hospital Civil of Guadalajara, we followed-up for 10 days AKI patients in whom a nephrology consultation was requested. We analyzed 5 early interventions of the nephrology team (fluid adjustment, nephrotoxic withdrawal, antibiotic dose adjustment, nutritional adjustment and removal of hyperchloremic solutions) after propensity score and multivariate analysis for the risk of starting KRT (primary objective), AKI progression to stage 3 and death (secondary objectives).
Results
From 2017 to 2020 we analyzed 288 AKI patients. The mean age was 55.3 years, 60.7% were male, AKI KDIGO stage 3 was present in 50.5% of them, sepsis was the main etiology 50.3%, and 72 (25%) patients started KRT. The overall survival was 84.4%. Fluid adjustment was the only intervention associated with a decreased risk for starting KRT (OR 0.58, 95% CI 0.48-0.70, p = <0.001) and AKI progression to stage 3 (OR 0.59, 95% CI 0.49-0.71, p = <0.001). Receiving vasopressors and KRT were associated with mortality, but neither of these interventions reduced these risks.
Conclusions
In this prospective cohort study of AKI patients, we found for the first time that early nephrologist intervention and fluid prescription adjustment was associated with a reduction in the risk of starting KRT and progression to AKI grade 3.

Figure 3. Forest plot of early nephrologist intervention associated with KRT and death.



KRT, kidney replacement therapy; OR, odd ratio; CI, confidence interval

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Staging of Sepsis-Associated Acute Kidney Injury using Markers of Function and Stress

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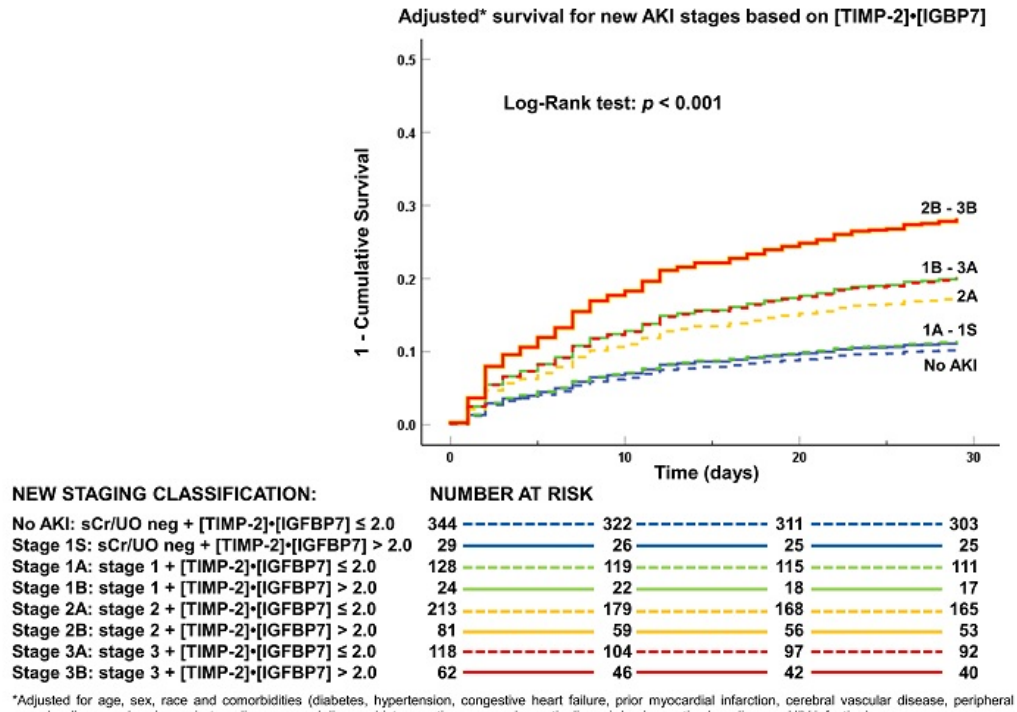
Purpose. Acute Kidney Injury (AKI) definition and severity staging is currently based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria that use two functional markers, serum creatinine (sCr) and urine output (UO). However, recent evidence suggests that urinary biomarkers may help identify patients at higher risk of adverse kidney outcomes within the same stage of AKI and also in patients without standard functional criteria for AKI. The 23rd Acute Disease Quality Initiative (ADQI-23) workgroup proposed an expanded classification for AKI adding biomarkers for each stage, and we tested if biomarkers of kidney stress, tissue

inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor-binding protein-7 (IGFBP7) could aid AKI staging.
Methods. We evaluated a cohort of critically ill patients with septic shock enrolled in a prior multicenter study of alternative fluid resuscitation strategies (ProCESS trial). We examined the presence and stage of AKI within 24 hours from enrollment. We used a previously defined "high specificity" cutoff for [TIMP-2]x[IGFBP7] of 2.0 (ng/mL)^2/1000 and, as proposed by ADQI-23, we redefined KDIGO standard AKI stages splitting each of them according to [TIMP-2]x[IGFBP7] <= 2.0 or > 2.0 (no AKI and stage 1S, stage 1A and 1B, stage 2A and 2B, stage 3A and 3B). Our primary endpoint was survival to 30 days, and it was assessed with Kaplan-Meier plots (Log-Rank test) and adjusted using Cox proportional-hazard models.
Results. We analyzed data on 999 patients with available data for sCr, UO and [TIMP-2]x[IGFBP7]. The use of [TIMP-2]x[IGFBP7] identified significantly different 30-day survival patterns (Log-Rank test p<0.001). Patients within the same functional AKI stage but with [TIMP-2]x[IGFBP7] > 2.0 had decreased survival compared to those with [TIMP-2]x[IGFBP7] <= 2.0 (Log-Rank test p<0.05 for all comparisons: stage 1A vs. 1B, stage 2A vs. 2B, and stage 3A vs. 3B). In absence of functional criteria for AKI, the presence of [TIMP-2]x[IGFBP7] > 2.0 did not portent different survival (p=0.70 for no AKI vs. stage 1S).
Conclusions. Biomarkers of kidney stress can aid AKI staging in patients who have already developed AKI identifying patients at higher risk of death.



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Non-resuscitation Fluid in Excess of Hydration Requirements is Associated with Higher Mortality in Critically Ill Children

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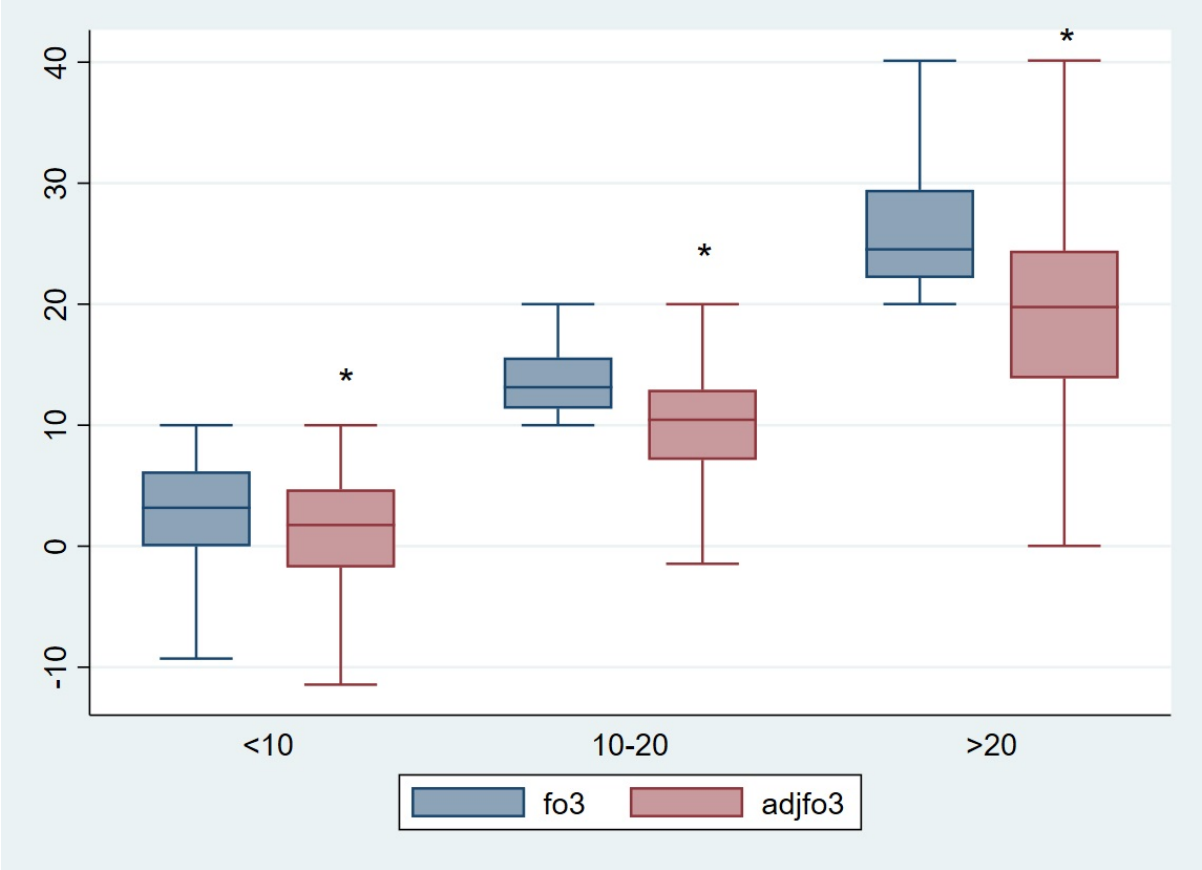
Background: Large volumes of non-resuscitation fluids are often administered to critically ill children. We hypothesize that excess maintenance fluid is a significant contributor to non-resuscitation fluid and that non-resuscitation fluid administered beyond hydration requirements is associated with worse clinical outcomes in critically ill children.
Methods: We evaluated all patients admitted to two large urban pediatric intensive care units (PICU) between 1/2010-8/2016 and 1/2010- 8/2018, respectively, who survived and remained in the hospital for at least 3 days following PICU admission. The primary outcome was in-hospital mortality. Association of excess fluid with outcomes was adjusted for confounders (age, PRISM III score, study site, and PICU era, resuscitation volume, and volume output) using multivariable regression.
Results: We evaluated 14,483 patients; 52% received non-resuscitation fluid in excess of hydration requirements. Non-resuscitation fluid in excess of hydration requirements was associated with higher in-hospital mortality after adjustment for confounders (adjusted odds ratio 1.01 per 10mL/kg in excess fluid, 95% confidence interval: 1.01-1.02).
Conclusions: Non-resuscitation fluid in excess of hydration requirements is associated with increased mortality in critically ill children. Excess maintenance fluid is a modifiable contributor to this fluid volume. Strategies to reduce excess maintenance fluids warrant further study.



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Recalibration of the Renal Angina Index to Predict Severe Acute Kidney Injury in Pediatric Septic Shock

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Purpose: Acute kidney injury (AKI) is a common complication of pediatric sepsis that is associated with poor outcomes. Unfortunately, the treatment of sepsis-associated AKI remains limited to supportive care, highlighting the need for early identification of at risk patients to facilitate proactive intervention. The Renal Angina Index (RAI) is a validated tool for the prediction of severe AKI in general populations of critically ill children, however, data regarding its performance in sepsis remain limited. We sought to assess the ability of the RAI to predict the presence of severe AKI on day 3 of pediatric septic shock (severe D3 SA-AKI).

Methods: We performed an analysis of a prospective study of children admitted to 14 pediatric intensive care units (PICUs) from 2015 to 2018 with septic shock. The RAI (Figure 1) was calculated from clinical data collected within the first 24 hours. The primary outcome assessed was the ability of the RAI to predict the development of severe D3 SA-AKI (≥ KDIGO Stage 2), and a Youden Index was calculated to determine the optimal cutoff point for this prediction. Secondary outcomes assessed included RRT use, D3 fluid overload >20% (FO), PICU length of stay (LOS) and mortality.

Results: Among 379 patients, 65 (17.2%) developed severe D3 SA-AKI. The RAI had an AUROC of 0.90 (0.86-0.93, <0.0001) for the prediction of severe D3 SA-AKI. Using the previously validated cutoff of ≥8 to define RAI+ yielded a sensitivity of 0.98, specificity 0.55, PPV 0.31 and NPV 0.99. A Youden Index revealed an optimal cutoff point of ≥20, with an associated sensitivity of 0.83, specificity 0.80, PPV 0.47, and NPV 0.96. Using either cutoff, being RAI+ was associated with significantly higher risk of D3 FO, RRT use, mortality, and prolonged PICU LOS, compared to RAI-. Patients who developed severe D3 SA-AKI had lower initial platelet counts compared to those who did not (median 78 [26,154] vs. 167 [86,263], p<0.001), and the requirement of platelet count <150 to define RAI+ in patients with intermediate RAIs (8 to ≤20) yielded a sensitivity of 0.95, specificity 0.69, PPV 0.39 and NPV 0.99.

Conclusions: At the typical cutoff of ≥8, the RAI predicts the development of severe D3 SA-AKI with high sensitivity but poor specificity. Our analyses suggest a higher threshold of ≥20 may improve specificity, and that recalibration of the RAI to incorporate admission platelet count may be appropriate for SA-AKI prediction.

Risk Strata: Select highest that applies

Risk Criteria	Score
PICU Admission	1
History of transplantation (solid organ or stem cell)	3
Mechanical ventilation AND vasoactive support	5

Injury Strata: Select highest that applies

SCr/Baseline or	% FO	Score
Decreased or no change	<5%	1
>1x – 1.49x	5-10%	2
1.5x – 1.99x	10-15%	4
≥ 2x	>15%	8

Risk x Injury = RAI (Scores: 1-40)

Figure 1. The Renal Angina Index (RAI). Calculated as the product of the highest risk and injury strata, a score of ≥ 8 has been previously defined as fulfillment of renal angina and validated to predict the presence of severe AKI 3 days later. Adapted from: Basu et al, Lancet Child Adolesc Health (2018).

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The PERSEVERE-II Model Outperforms the Renal Angina Index for Severe Acute Kidney Injury Prediction in Pediatric Septic Shock

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Purpose: Acute kidney injury (AKI) occurs commonly in pediatric septic shock and is associated with substantial morbidity and mortality. Unfortunately, current management relies solely on supportive care, highlighting the need for reliable tools for early identification of high risk patients. Currently, the Renal Angina Index (RAI)

is the only validated tool for prediction of severe AKI in critically ill children, although its study in sepsis is limited. We have previously published the PERSEVERE-II Model—which incorporates day 1 serum creatinine and sepsis biomarkers— for prediction of severe AKI on day 3 of septic shock (severe D3 SA-AKI). We sought to assess the performance of this model in comparison to and in combination with the RAI.

Methods: We performed an analysis of a prospective study of children admitted to 14 pediatric intensive care units from 2015 to 2018 with septic shock. Patients were assigned an RAI and a probability of severe D3 SA-AKI via the PERSEVERE-II Model based on day 1 clinical and laboratory data. Patients were RAI+ if RAI ≥8; they were PERSEVERE+ if they were predicted to have severe D3 SA-AKI by the PERSEVERE-II Model. The primary outcome was the development of severe D3 SA-AKI (≥ KDIGO Stage 2). The performance of each model was assessed for comparison using receiver operating curves.

Results: Of 379 patients, 65 (17.2%) developed severe D3 SA-AKI. 207 patients (54.6%) were RAI+ and 94 (24.8%) were PERSEVERE+. The PERSEVERE-II Model was superior to the RAI for prediction of severe D3 SA-AKI (AUC 0.95 vs. 0.90, p=0.008) (Table 1). 82 patients were both RAI+ and PERSEVERE+, and 59/82 (72%) developed severe D3 SA-AKI. RAI+PERSEVERE+ predicted the presence of severe D3 SA-AKI with the test characteristics outlined in Table 1, including a +LR of 12.4.

Conclusions: Among children with septic shock, the sepsis-specific PERSEVERE-II Model appears to outperform the RAI for the prediction of severe D3 SA-AKI. Additionally, targeted measurement of the PERSEVERE-II Model in RAI+ positive patients appears to be feasible and possibly increases the predictive performance.

Variable	RAI	PERSEVERE-II	Comparison	RAI+PERSEVERE+
AUC	0.90 (0.86-0.93)	0.95 (0.92-0.98)	p=0.008	--
Sensitivity	98 (91-99)	92 (82-97)		91 (80-96)
Specificity	54 (49-60)	89 (85-92)		93 (89-95)
PPV	31 (25-38)	64 (53-73)		72 (61-81)
NPV	99 (96-99)	98 (96-99)		98 (95-99)
+LR	2.2 (1.9-2.4)	8.5 (6.2-11.8)		12.4 (8.3-18.5)
-LR	0.03 (0.004-0.20)	0.09 (0.04-0.20)		0.10 (0.05-0.21)

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COVID-19 PATIENTS WITH ACUTE KIDNEY INJURY (AKI) BIOMARKER POSITIVE (BM): PROFILING URINE CYTOKINES

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Introduction: Inflammatory cytokines could cause AKI.

Methods The study was conducted at the National Institute of Respiratory Diseases.The aim was to investigate the behavior of BM´s of kidney damage (neutrophil gelatinase-associated lipocalin[NGAL], urine tissue inhibitor of metalloproteinases-2 [TIMP-2] and insulin-like growth factor-binding protein 7 [IGFBP7]) and a panel of cytokines in urine of patients hospitalized with COVID-19. Three AKI groups were created using clinical assessment and validated BM´s(Recommendations of ADQI 23 Working Groups and Assignment). Group No-AKI (No change or sCr level increase <0.3 mg/dL and BM -), Group AKI BM + (1S, 1B, 2B, 3B), Group AKI BM – (1A, 2A, 3A). AKI BM+ was considered with a N-Gal value>100 ng/ml or (TIMP2/IGFBP7)/1000> 0.20.
We included individuals with severe pneumonia from May to August 2020 caused by SARS-CoV-2; 18 years of age or older; with no history of chronic kidney disease (CKD), and ratio of partial arterial oxygen pressure/inspired oxygen fraction (PaO 2 /FiO 2)< 300 mm Hg on admission. Clinical, laboratory and outcome records were recorded until discharge from the hospital. Urine samples were collected in the first 24 hours and 5 days after admission to the hospital. Samples were immediately stored at –80ºC until use.
Cytokine and Chemokine Quantification in urine were measured with a Luminex 200 instrument;ELISA technique was used for TIMP-2 and IGFBP7 and the plataform Architect® (Abbott) for N-Gal.
Analisis: We performed descriptive statistics including means and standard deviations(SD) for normally distribuited constinuous variables, medians and interquartile ranges for non-parametric distributions, and proportions for categorical variables. Comparisons across AKI stages were made using Kruskall Wallis rank sum test.

Results: 51 patients were analyzed,25 NO-AKI, 22 BM(+) and 4 BM(-), systemic arterial hypertension was significantly higher in patients with AKI.The profile of

cytokines, BM of AKI are shown in table 2.
AKI BM + was associated with increased expression of RANTES at baseline (p=0.03) and MCP-1 at day 5 (p=0.015) . In contrast urinary epidermal growth factor (EGF) levels were significantly higher in patients without AKI (p=0.046).
Conclusion:Cytokine behavior could be involved in the development of AKI BM +.

	NO AKI	AKI BM +	AKI BM -	p
Urine NGAL (ng/ml)				
Baseline	32.95 (14.10-40.80)	127.10 (57.05-298.10)	49.95 (14.80-97.60)	<0.01
Day 5	46.35 (17.70-59.70)	142.40 (14.00-270.80)	25.55 (18.40-32.70)	0.004
IGFBP-7 (ng/ml)				
Baseline	11.34 (7.81-17.73)	29.08 (14.26-47.99)	21.20 (9.91-27.61)	0.009
Day 5	14.29 (12.20-22.12)	106.02 (14.99-197.06)	18.23 (8.04-28.43)	<0.01
TIMP-2 (ng/ml)				
Baseline	5.04 (3.02-6.50)	6.96 (3.94-15.00)	5.42 (7.52-9.03)	0.185
Day 5	3.76 (3.30-3.87)	6.82 (5.78-7.86)	6.59 (5.41-7.76)	0.830
(TIMP-2/IGFBP-7)/1000				
Baseline	0.058 (0.035-0.088)	0.33 (0.17-0.44)	0.16 (0.06-0.24)	0.001
Day 5	0.05 (0.04-0.08)	0.82 (0.09-1.55)	0.10 (0.06-0.15)	0.006
FGF				
Baseline	3.03 (1.44-7.95)	1.86 (0.98-6.64)	2.29 (1.06-9.13)	0.660
Day 5	3.05 (0.74-10.99)	1.08 (0.74-1.42)	1.57 (1.14-1.99)	0.807
IL1B				
Baseline	10.41 (5.10-20.11)	6.04 (2.58-11.37)	7.24 (1.85-15.65)	0.448
Day 5	9.78 (5.92-12.45)	7.31 (7.02-7.60)	7.25 (2.22-12.29)	0.622
GCSF				
Baseline	133.83 (8.62-188)	8.62 (8.62-42.32)	63.69 (8.62-157.38)	0.124
Day 5	90.29 (64.69-216.52)	14.16 (8.62-19.70)	59.06 (8.62-109.50)	0.850
IL-6				
Baseline	7.85 (2.80-17.17)	7.78 (4.73-15.43)	5.00 (3.17-9.94)	0.487
Day 5	6.60 (2.71-11.16)	38.09 (5.92-70.27)	5.94 (5.15-6.74)	0.241
RANTES				
Baseline	2.06 (2.06-12.53)	17.32 (8.77-24.50)	10.13 (2.06-14.76)	0.030

Day 5	2.06 (2.06-15.27)	2.06 (2.06-14.62)	17.95 (5.59-30.31)	0.448
GMCSF				
Baseline	0.67 (0.38-1.28)	0.80 (0.45-1.23)	0.50 (0.32-1.00)	0.124
Day 5	0.96 (0.60-1.51)	1.19 (0.49-1.89)	1.49 (1.19-1.78)	0.056
MIP1b				
Baseline	2.91 (1.84-8.16)	2.94 (2.62-6.09)	2.51 (1.76-9.15)	0.923
Day 5	2.38 (0.80-6.15)	6.83 (6.27-7.40)	3.25 (1.37-5.14)	0.090
MCP1				
Baseline	120.97 (49.18-222.41)	195.62 (129.58-359.90)	117.88 (50.48-290.41)	0.339
Day 5	126.94 (104.36-164.14)	1249.91 (119.71-2380.11)	160.33 (91.46-229.20)	0.015
EGF				
Baseline	4581 (4581-5523)	4581 (2044-4581)	4354 (2096-4581)	0.046
Day 5	4581 (4581-5694)	3737 (2780-4694)	3198 (1382-5013)	0.493
VEGF				
Baseline	2.73 (0.59-4.20)	2.20 (0.82-3.79)	2.73 (0.655-5.07)	0.962
Day 5	2.16 (1.07-4.36)	3.06 (3.01-3.10)	1.86 (1.49-2.24)	0.926
TNFa				
Baseline	0.55(0.55-1.96)	0.55(0.55-0.55)	0.55(0.55-1.35)	0.705
Day 5	0.55 (0.55-1.85)	1.02 (0.55-1.49)	1.40 (1.39-1.42)	0.212
IL-2				
Baseline	1.61(1.50-2.23)	1.61(1.40-1.83)	1.60(1.54-1.61)	0.611
Day 5	1.61 (1.61-1.61)	2.53 (1.61-3.45)	2.79 (1.95-3.63)	0.227

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Biomarker and Safety Results from a Phase 1b Dose-Escalating Study of RBT-1 in Healthy Volunteers and Subjects with CKD Stage 3/4

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Purpose of the Study:
RBT-1 is a novel therapeutic designed to induce renal preconditioning and prevent acute kidney injury (AKI) induced by multiple injurious pathways. It is composed of proprietary formulations of stannous protoporphyrin (SnPP) and iron sucrose (FeS), which act in concert to evoke protection by upregulating antioxidant and anti-inflammatory pathways.

This Phase 1b study was designed to assess the safety and tolerability of RBT-1 in healthy volunteers and subjects with chronic kidney disease (CKD) Stage 3/4. It was also designed to validate RBT-1's effects on cytoprotective biomarker responses, as observed in experimental animals.

Methods Used:
A total of 54 subjects (18 healthy volunteers and 36 subjects with CKD Stage 3/4) were enrolled and received a single intravenous dose of RBT-1 (240 mg FeS plus SnPP at 9, 27, 45, 63, or 90 mg) over 120-minutes. Cytoprotective antioxidant proteins (plasma heme oxygenase-1 [HO-1] and ferritin) and anti-inflammatory interleukin-10 (IL-10) were measured from baseline through 168 hours post-dose. Safety was assessed for 28 days.

Summary of the Results:
RBT-1 markedly and significantly upregulated HO-1, ferritin, and IL-10 in both healthy volunteers and subjects with CKD, indicating cytoprotective responses. A total of 35 TEAEs were reported 23 subjects. The majority of the TEAEs (n=17; 49%) were photosensitivity-related events. In general, photosensitivity AEs were mild, with 4 considered moderate and only 1 considered severe. Most resolved by the end of study (within 28 days). There were no deaths, SAEs, or study drug discontinuations. There was no evidence of renal injury, as assessed by stable levels of serum creatinine and urine albumin and the absence of increases in renal tubular injury biomarkers

(KIM-1, NGAL, cystatin C, NAG). No evidence of liver or cardiac injury (as assessed by liver transaminases and troponin I levels) was observed in any subject.

Conclusions:
RBT-1 was well-tolerated in both healthy volunteers and subjects with CKD. Adverse events were generally mild and related to photosensitivity reactions. Cytoprotective responses were observed following RBT-1 administration, corresponding with previously observed AKI protection in experimental animals. A Phase 2 study is planned to assess the safety and efficacy of RBT-1 on preconditioning response biomarkers and AKI prevention in subjects undergoing coronary artery bypass graft and/or cardiac valve surgery (NCT04564833).

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Non-Cardiac Post-Operative Acute Kidney Injury and Association with Elevated Urinary Neutrophil Gelatinase Associated Lipocalin in Neonates

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Background: Non-cardiac surgical intervention is a risk factor for acute kidney injury (AKI) in neonates yet remains understudied. Urine neutrophil gelatinase-associated lipocalin (uNGAL) is a widely used predictive biomarker for AKI, however it is applied rarely in the neonatal intensive care unit. The objective of this study was to characterize and assess the ability of uNGAL to predict post-operative AKI in neonates.

Methods: Infants undergoing high-risk non-cardiac surgical procedures were prospectively enrolled from October 2018 to March 2020. uNGAL was measured at 7 time points: pre-op and 12, 24, 36, 48, 72 and 96 hours post-op. AKI was defined by the neonatal modified Kidney Diseases: Improving Global Outcomes (KDIGO) definition. Samples were processed using The NGAL Test® (BioPorto, Denmark). Performance of post-operative uNGAL to predict AKI following procedures was

determined using sensitivities, specificities, and area under the receiver operator curves (AUC-ROC). Risk factors for AKI were identified in univariate analysis using Chi-square analysis for categorical variables and the Wilcoxon rank test for continuous variables. Adjusted odds ratios (aOR) for mortality in subjects were calculated with 95% confidence intervals.

Results: 141 neonates underwent 192 surgical procedures. AKI occurred in 18% (36/192). Twenty-three subjects met criteria by urine output, 8 by serum creatinine (SCr), and 5 by both criteria. Risk factors for AKI following procedures included: prior history of AKI (42% vs 20%, p=0.025), pre-op nephrotoxic medication exposure (37% vs 19%, p=0.032), increased SCr monitoring (5 [4,8] vs 3 [2,4] per 5 days, p<0.0001), and emergent procedure (64% vs 30%, p=<0.001). Following procedures, infants with AKI had higher uNGAL concentrations at all post-op time points (Table 1), which remained true when patients with pre-operative AKI were excluded. The best uNGAL performance to predict AKI was at 24 hours post-op (AUC-ROC 0.81; 95%CI: 0.72-0.89). Subjects with post-op AKI had increased risk for mortality by discharge (aOR 11.1; 95%CI: 2.0-62.8; p=0.0063).

Conclusion: Post-op AKI is common following surgical procedures and is associated with increased risk for mortality. uNGAL offers clinical utility with excellent predictive probability at 24 hours for AKI following procedures.

Table 1. Median (IQR) uNGAL concentrations (ng/mL) in No AKI vs. AKI							
	Pre-op	12-hour	24-hour	36-hour	48-hour	72-hour	96-hour
	(n=119)	(n=153)	(n=165)	(n=163)	(n=161)	(n=163)	(n=146)
No AKI (n=156)	26 (9,101)	27 (11, 120)	38 (12, 160)	39 (14, 131)	42 (14, 123)	33 (13, 92)	32 (10, 89)
AKI (n=36)	59 (14, 174)	244 (18, 1410)	292 (164, 2440)	243 (82, 1890)	290 (42,2030)	132 (41, 419)	131 (44, 442)
p value	0.1181	0.0009	<0.0001	<0.0001	0.0004	0.0004	<0.0001

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Effects of Hyperuricemia, Hyperlipidemia And Overweight On The Incidence Of Acute Kidney Injury Following Cardiac Surgery

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Background Acute kidney injury (AKI) remains a common complication of cardiac surgery and some risk factors may be superimposed on it. For example, hyperuricemia is an independent risk factor of AKI, and patients with hyperuricemia are often accompanied with metabolic disorders. This study intends to explore the effects of hyperuricemia, overweight and hyperlipidemia on the incidence of AKI in patients following cardiac surgery.
Methods Clinical data of patients underwent cardiac surgery from July 2015 to December 2015 in our hospital were retrospectively collected. Pearson correlation was used to analyze the correlation between uric acid, lipids and body mass index(BMI), and multivariate logistic regression analysis was used to analyze the risk factors of postoperative AKI. Patients were grouped by quartiles of uric acid levels.
Results A total of 1420 patients were enrolled. The AKI incidence was higher in higher uric acid quartiles ($p<0.001$). Patients in the higher uric acid quartiles were more likely to have overweight and hyperlipidemia. Pearson correlation analysis showed that there was a positive correlation between uric acid and triglyceride levels ($r=0.221$ $p<0.001$), and with BMI ($r=0.157$, $p<0.001$), and a negative correlation with HDL-c ($r=0.190$, $p<0.001$). Multivariate Logistic regression analysis showed that hyperuricemia was an independent risk factor for AKI (OR=1.237, 95%CI 1.095-1.885, $p=0.009$), and when it existed, overweight or hyperlipidemia alone was not independent risk factor, but the combination of overweight and hyperlipidemia was. In the final model, the OR value increased to 3.126 when hyperuricemia combined with overweight and hyperlipidemia, and Hosmer and lemeshow test showed that the model fitted well ($p=0.597$).
Conclusion There were correlations between uric acid with blood lipids and BMI. Overweight or hyperlipidemia alone was not independent risk factor for AKI, but the combination of overweight and hyperlipidemia was. The superposition of hyperuricemia, overweight and hyperlipidemia further increased the risk of AKI following cardiac surgery.

	All (n=1420)	Q1 (n=351)	Q2 (n=360)	Q3 (n=353)	Q4 (n=356)	P
Gender (male) [n(%)]	833(58.7%)	127(36.2%)	207(57.5%)	231(65.4%)	272(76.4%)	<0.001
Age	57.1±12.2	56.7±12.5	56.9±12.3	56.9±12.4	57.7±11.5	0.877
BMI(kg/m2)	23.6±3.3	22.9±3.2	23.2±3.2	24±3.2	24.4±3.4	<0.001
Overweight [n(%)]	601(42.3%)	108(30.8%)	131(36.4%)	170(48.2%)	192(53.9%)	<0.001
Hypertension [n(%)]	532(37.5%)	113(32.2%)	127(35.3%)	141(39.9%)	151(42.4%)	0.023
Diabetes[n(%)]	221(15.6%)	56(15.9%)	55(15.3%)	57(16.1%)	53(14.9%)	0.228
BUN (mmol/L)	6.0±2.0	5.2±1.5	5.7±1.5	6±1.8	7.2±2.6	<0.001
SCr (μmol/L)	80.8±22.4	67.7±15.3	76.6±14.6	82.1±16.6	96.6±29.1	<0.001
eGFR [ml/(min/1.73m2)]	86.4±20.6	97.3±20.1	89.1±18.1	84.7±18.5	74.7±19.3	<0.001
eGFR<60ml/(min/1.73m2) [n(%)]	117(8.2%)	7(2.0%)	13(3.6%)	27(7.6%)	70(19.7%)	<0.001
Cholesterol (mmol/l)	4±0.9	4±0.9	4±0.9	4.1±0.9	4±0.9	0.073
Triglyceride (mmol/l)	1.3±0.8	1.1±0.6	1.3±0.7	1.5±1	1.5±0.9	<0.001
LDL-c(mmol/l)	2.3±0.8	2.2±0.8	2.2±0.8	2.4±0.8	2.3±0.8	0.132
HDL-c(mmol/l)	1.2±0.3	1.3±0.4	1.2±0.3	1.1±0.3	1.1±0.4	<0.001
Hyperlipidemia [n(%)]	292(20.6%)	36(10.3%)	68(18.9%)	86(24.4%)	102(28.7%)	<0.001
Blood glucose(mmol/L)	5.2±0.7	5.4±1.8	5.3±1.7	5.3±1.4	5.3±1.4	0.788
Albumin(g/L)	40.8±3.9	39.1±3.4	39.7±3.3	40.1±3.6	40.4±3.8	<0.001
Coronary angiography[n(%)]	691(48.7%)	165(47.0%)	176(48.9%)	174(49.3%)	176(49.4%)	0.519

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Risk Scoring Systems including Electrolyte Disorders for Predicting the Incidence of Acute Kidney Injury in hospitalized patients

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Introduction: Electrolyte disorders were common among patients with acute kidney injury (AKI) and adversely affect the outcome. So far, various clinical scoring systems to predict AKI haven't involved electrolyte disorders. This article emphasized on the potential role of abnormal electrolyte levels on predicting AKI and severe AKI.
Methods: In this retrospective and observational study, we included all subjects admitted to Zhongshan Hospital, Shanghai Medical college, Fudan University from October 01, 2014 to September 30, 2015. Since only a few patients underwent arterial blood gas analysis (ABG), all subjects involved were divided into two groups: patients with ABG and patients without ABG. Severe AKI was defined as AKI stage 2 or 3 according to KDIGO guideline.
Results: A total of 57264 patients were enrolled prospectively and distributed randomly into two cohorts. The derivation cohort consisted of 38107 patients, and the validation cohort consisted of 19157 patients. Among the derivation cohort, logistic regression was used to analyze risk factors including electrolyte disorders that were associated with AKI and severe AKI. Among the validation cohort, the point scoring of risk factor combinations led to AUC values of 0.710 (AKI with ABG), 0.734 (AKI without ABG), 0.723 (severe AKI with ABG), 0.811 (severe AKI without ABG), and Hosmer–Lemeshow tests revealed a good agreement of expected and observed AKI rates.
Conclusions: The novel risk scoring systems involving electrolyte disorders were established to predict AKI and severe AKI. Electrolyte imbalance should be carefully monitored and corrective measures should be taken on time to avoid further serious commodities.

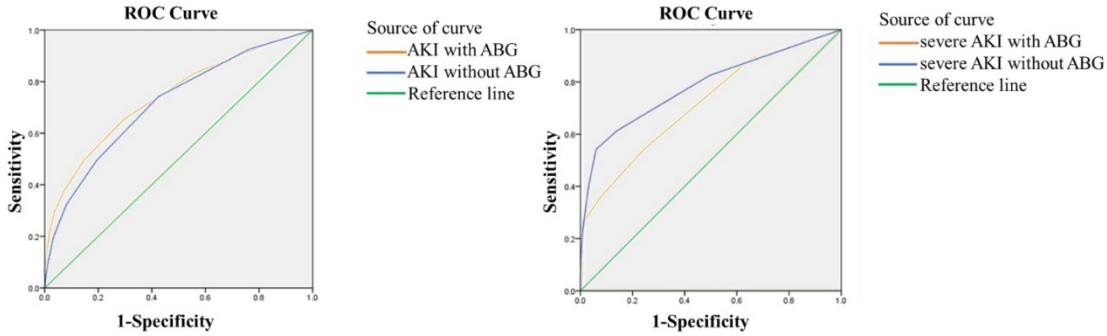

Fig. 2. a. AKI with and without ABG

Fig. 2. b. severe AKI with and without ABG

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Development of a Population Pharmacokinetic Model of Teicoplanin in Chinese Adult Patients with Gram-Positive Cocci Infections

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Background
Teicoplanin is used for the treatment of infections caused by gram-positive cocci. Although studies have shown that teicoplanin has lower renal injury than other glycopeptide antibiotics, teicoplanin-induced acute kidney injury(AKI) still should be paid more attention as the dosage has increased in some serious infection which may cause more AKI that can significantly increase the mortality and medical expenses. Therefore, we should design individualized administration regimen to ensure the efficacy and reduce the incidence of kidney injury.

Methods
This study was conducted at Peking University First Hospital to estimate the population pharmacokinetics of teicoplanin in Chinese adult patients. The main study inclusion was aged ≥18 years, inpatients at Peking University First Hospital, received intravenous teicoplanin infusion due to gram-positive cocci infections, and signed the informed consent. Principal exclusion criteria included lacking therapeutic drug monitoring of teicoplanin. The steady-state trough concentrations were retrospectively collected from May 2018 to September 2018 and were analyzed using the Nonlinear Mixed-Effect Model software. The final model was evaluated using the bootstrap method, goodness-of-fit plots and the normalized prediction distribution error method.

Results

In this study, 249 plasma sampling from a total of 59 subjects were collected. Two-compartment model successfully described the data. The model estimated the parameter clearance (CL), central volume(V1), inter-compartmental clearance(Q) and peripheral compartment volume (V2). After the stepwise covariate modeling, Glomerular Filtration Rate (gfr) effected on the CL of teicoplanin. CL was described as a function of mmf by using equation (1) and equation (2), where TVCL(1.03 L/h) is the population parameter of CL, θ(CL_gfr) is 0.437.

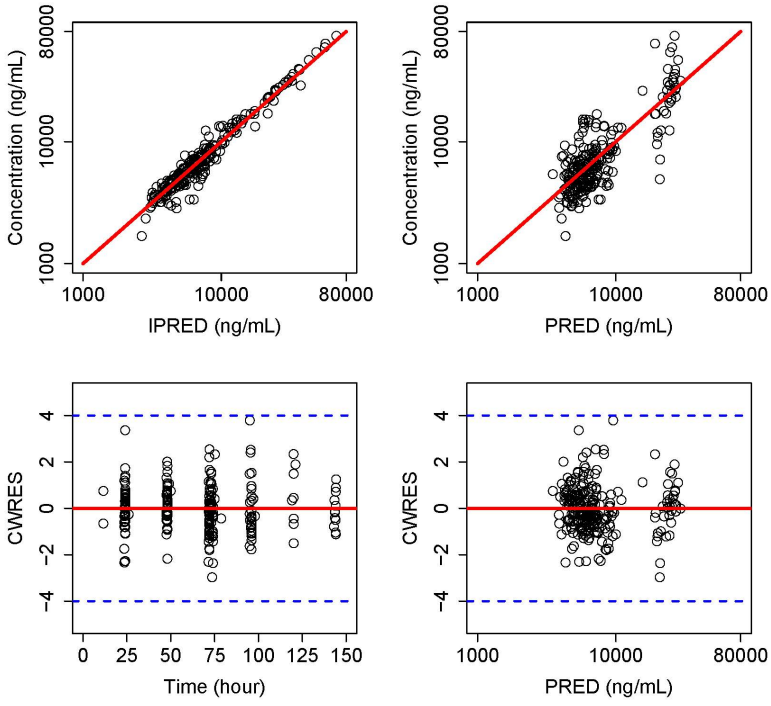
CL=TVCL* COV(CL_gfr) (1)

COV(CL_gfr)=(gfr/71.88)^θ(CL_gfr) (2)

The final model was validated by nonparametric bootstrap, and the final model demonstrated strong stability.

Conclusion

A population pharmacokinetic model of teicoplanin was established to estimate the pharmacokinetics characteristics of Chinese adult patients with gram-positive cocci infections, and this model can be used to develop an initial teicoplanin dosing regimen for patients, which can ensure the efficacy and reduce the incidence of acute kidney injury at the same time.



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Predictors of Mortality in Severe Leptospirosis with Acute Kidney Injury

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Purpose of the Study: The Philippines has a high incidence and mortality rate from severe leptospirosis with acute kidney injury and pulmonary hemorrhage. There is a need for a predictive scoring system to identify those who require aggressive management and intensive monitoring. This study is an external validation of the 4-point DIVA clinical score developed at the National Kidney and Transplant Institute, Philippines.

Methods: This is a retrospective cohort of adult patients with moderate to severe Leptospirosis admitted between January 2019 and September 2020. The 4-point DIVA score (diabetes, icterisia, ventilation, anuria/oliguria) was applied to eligible patients. Outcomes were reported and Area under the Curve (AUC) was computed.

Results and Discussion: Among 151 patients diagnosed with leptospirosis based on Latex Agglutination Test (LAT) or Microagglutination Test (MAT) which were included in the study, mortality rate was found to be at 5.9%. Majority of patients (88.4%) required renal replacement therapy and 2.9% of them underwent Continuous Renal Replacement Therapy (CRRT). Both Extracorporeal Membrane Oxygenation (ECMO) and Hemoperfusion (HP) were performed in 19.27% of the patients. Patients who expired were significantly younger, had shorter hospital stay since they died early in their hospital course, lower baseline blood pressure and had hemoptysis within 24 hours of admission compared to those who survived. The DIVA score had an AUC of 0.9601 with excellent discriminative capability. Recommended cut off score was > 7 with sensitivity of 100% and specificity of 94.37%.

Conclusion: A DIVA score of >7 showed a very high accuracy to predict mortality in patients with moderate to severe leptospirosis. A high DIVA score can select patients that will require rigorous monitoring and management to improve survival.

Table 1. DIVA Scoring System from Capucion *et al.* (2019)

PREDICTOR		
DIABETES MELLITUS	Absent	0
	Present	2
JAUNDICE	Absent	0
	Present	1
RESPIRATORY SUPPORT	Without	0
	Non-invasive	2
	Invasive	5
URINE OUTPUT	Normal	0
	Oliguric	1
	Anuric	2

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Genome-Wide Association Study of Vancomycin-induced Acute Kidney Injury

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Background
Vancomycin is the first-line treatment for methicillin-resistant staphylococcus aureus (MRSA) caused infections. Acute kidney injury (AKI) is a common adverse drug reaction of vancomycin which is associated with increased mortality and morbidity. Vancomycin-induced AKI may be influenced by exposure and mechanisms involved in renal excretion and reabsorption, some of which may be under genetic control. The aim of this study was to explore the potential genetic risk factors of vancomycin induced AKI.
Methods
This study was a multicenter trial which included adult patients using vancomycin in 7 hospitals in China. The participants were recruited from November 1st, 2018, to December 31st, 2019. The main study inclusion was aged ≥18 years inpatients, received intravenous vancomycin infusion due to infections, and signed the informed consent. Principal exclusion criteria included multiple organ failure, renal replacement therapy, or chronic kidney disease stages 4 or 5. Patients withdrew when used vancomycin for less than 48 h. Clinical information and blood samples were collected from all patients and AKI judgment follows KDIGO guidelines. DNA samples were

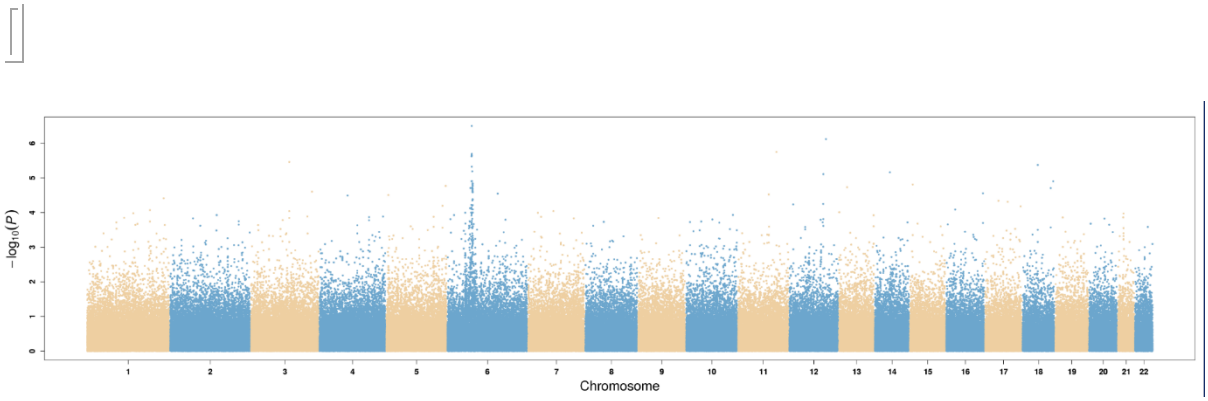
genotyped on the CBC-PMRA 96-Array Plate and were divided into AKI group (case) and non-AKI group (control), with gender and age as the correction factors for the follow-up data analysis.

Results

A total of 576 eligible patients were screened, of which 490 patients were in the control group and 86 patients were in the case group. Plink1.90 was used for quality control of the original data, including sample deletion rate, site deletion rate, minor allele frequency (MAF), Hardy Weinberg equilibrium (HWE) test and PCA analysis. After deleting outlier samples, a total of 565 patients and 528924 SNPs were left. Analyses revealed three regions may associated with manganese level at genome-wide significance, mapping to 6p22, 6p21 and 6p23. The lead single nucleotide polymorphism (SNP) in the 6p22 locus was rs398123368 (P-value = 2.17 × 10(-10)), located in an exonic of LAMA2. The 6p21 locus was rs195418 (P-value = 5.84 × 10(-10)), located in an intronic of RNF8. The 6p23 locus were rs759748149(P-value = 1.09 × 10(-9)) and rs147790535(P-value = 1.14 × 10(-9)), located both in an exonic of SLC18B1.

Conclusions

Vancomycin-induced AKI may be associated with genetic variants. Our findings implicate novel risk genes and related pathway for further study.



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Electronic alerts system with automated consultation for acute kidney injury in children

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Introduction
Acute kidney injury (AKI) is a common and raising problem in hospitalized patients. AKI is often under-recognized by physicians and associated with higher morbidities and mortality. To improve clinical outcomes, an electronic alert system for AKI could be a useful tool for early diagnosis and intervention. Several AKI alert systems have been developed and reported in adults, but not children. To improve the quality of AKI care, we applied an electronic AKI alert system with automated consultation to all pediatric patients hospitalized in our children's hospital.
Methods and Analysis
We adopted an AKI alert system by confines of the electronic medical record system on July 2020. The AKI alert system was based on Kidney Disease Improving Global Outcomes (KDIGO) criteria. The system was programmed to activate again when the AKI stage increases or AKI recurs. Through implantation of this system, an automated consultation is generated and sent to the division of pediatric nephrology. Pediatric nephrologists respond to optimize management of AKI based on the assessment of overall clinical status, including the cause and risk of AKI, changes in kidney function over time, comorbid conditions, volume status, and concomitant acid-base and electrolyte disturbances. In addition, patients with AKI are encouraged to continue nephrology division follow-up after AKI.
We are planning to evaluate the effectiveness of this system by comparing clinical outcomes of pediatric patients who have AKI before and after launching of the system. The historical control group consists of index admission cases with the same criteria that were admitted in one year before the start of this system. Primary outcomes include AKI recovery, mortality, and the consultation pattern of attending clinicians, Secondary outcomes are severities of AKI events, rate of follow-up to pediatric nephrologists, kidney replacement therapy, and length of hospital stay.
Conclusion
We expect that our electronic AKI alert system with automated consultation contributes to not only shortening the delay from onset of AKI to an expert consultation, but also improving clinical outcomes of pediatric patients with AKI.

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Proenkephalin, Cystatin C, Creatinine and Measured GFR in ICU patients.

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Background: Assessing renal function in clinical settings such as intensive care unit (ICU) remains challenging and commonly used creatinine-based estimated glomerular filtration rate (GFR) equations are hampered by sarcopenia and are inaccurate for mild renal impairment. Measured GFR by means of iohexol or inulin clearance is laborious and time consuming, therefore rendering them unfit for daily clinical use in the ICU. Cystatin C has long offered a slightly better alternative to creatinine but still lacks sensitivity and may be interfered by states of immunosuppression, inflammation, malignancies, and disturbed thyroid function. Proenkephalin A 119-159 (penKid) is a novel biomarker which offers a quick and easily performed bedside estimate of kidney function. In smaller studies, penKid has shown to more accurately reflect the measured GFR when compared to commonly used creatinine-based eGFR methods. This pilot study aims to assess the performance of penKid as an estimator for GFR compared with GFR measured by iohexol in a cohort of ICU patients.

Materials and Methods: Twenty-eight critically ill patients with prolonged ICU treatment time were included. GFR was measured with multiple (fourteen) point iohexol plasma clearance and used as reference. Estimation of GFR was based on creatinine and cystatin C using recognized estimated GFR equations CKD-EPI, CAPA, and LM-rev. Concentrations of plasma penKid were measured with a validated chemiluminescence immunoassay (SphingoTec GmbH, Hennigsdorf, Berlin).

Results: All biomarkers were significantly correlated with measured GFR: penKid (r=-0.58), cystatin C (r=-0.89) and creatinine (r=-0.74). In linear regression analysis, penKid significantly improved estimated creatinine-based GFR equations CKD-EPI (p=0.0041), CAPA (p=0.0038), and LM-rev. (p=0.0054). Plasma levels of penKid were superior to measured GFR, cystatin C and creatinine in predicting 90-day mortality: C index 0.82 [95% confidence interval [CI] 0.64-1.0) for penKid compared to 0.80 (95% CI 0.68-0.92) for measured GFR, 0.72 (95% CI 0.67-0.92) for cystatin C and 0.64 (95% CI 0.48-0.80) for creatinine.

Conclusion: In this pilot study of steady-state critically ill ICU patients, penKid appears to be well associated with kidney function, adding to creatinine-based estimation of GFR. In addition, penKid showed to be the strongest predictor of 90-day mortality compared to both cystatin C and serum creatinine.

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The Outcomes of Comprehensive versus Standard Care in Post-Acute Kidney Injury Survivors: A Randomized Controlled Trial

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Background:
Survivors after severe acute kidney injury (AKI) are at high risk of progression to chronic kidney disease (CKD), and death. Comprehensive care of these patients may improve the outcomes.
Objectives:
We aimed to compare the feasibility outcomes between comprehensive follow-up care and standard care in AKI survivors.
Methods:
This open-labeled randomized controlled trial was conducted at King Chulalongkorn Memorial Hospital between August 2018 to December 2020. Patients who survived stage 3 AKI were enrolled and randomized to be follow up with comprehensive post-AKI care or standard care at 1, 3, 6, 9, and 12 months. The comprehensive post-AKI care integrates a multidisciplinary care team (nephrologists, nurses, nutritionists, and pharmacists). Primary outcomes were rate of loss to follow up, rate of specialist consultation, rate of 3-day dietary record, rate of drug reconciliation, and rate of drug alert at 12 months. Secondary outcomes included major adverse kidney events (MAKE), estimated glomerular filtration rate (eGFR), and albuminuria at 12 months.

We also reported the rates of blood pressure control, new episodes of systemic disease, quality of life, and mortality.

Results:

Eighty patients with stage 3 AKI were enrolled. Forty patients were randomized into comprehensive care groups. Compared to the standard group, the comprehensive care group had a lower rate of loss to follow up (43% vs 64%, p=0.068), significant higher rates of specialist consultation (100% vs 64%, p=0.006), 3-day dietary record (76% vs 0%, p<0.001), medical reconciliation (100% vs 0%, p<0.001), and drug alerts (33% vs 0%, p=0.01). Mean eGFR at 12 months were comparable between two groups (58.2 vs 57.8 mL/min/1.73m2, p=0.922). Urine albumin to creatinine ratio was significantly lower in the comprehensive care group (65.3 vs 352.2 mg/g, p=0.049). Quality of life was also better in the comprehensive care group, but not statistically significant. There was no difference in MAKE, blood pressure control, new episodes of systemic disease, and mortality at 12 months between the two groups.

Conclusion:

Comprehensive post-AKI care was feasible in order to improve patient outcomes. This integrated patient care could be implemented in clinical practice and should be further investigated in terms of long-term clinical outcomes.

	All (N=76)	Standard Care (N=39)	Comprehensive Care (N=37)	p-value
Loss F/U, N(%)	41 (54)	25 (64)	16 (43)	0.068
Specialist consultation, N(%)	30/35 (86)	9/14 (64)	21/21 (100)	**0.006**
3-day dietary recall, N(%)	16/35 (46)	0/14 (0)	16/21 (76)	**<0.001**
Drug reconciliation, N(%)	21/35 (60)	0/14 (0)	21/21 (100)	**<0.001**
Drug alert, N(%)	7/35 (20)	0/14 (0)	7/21 (33)	**0.027**

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A Knowledge Assessment of Frontline Healthcare Providers Awareness on Acute Kidney Injury on Hospitalized Patients, Educational Opportunities in Diagnosis and Management

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**CHOA/Emory, **Guys and Thomas, NHS, ***UC San Diego, ****IPSOS, *****bioMerieux, ******Vicenza*

Purpose: Acute kidney injury (AKI) is consistently associated with poor outcomes. Delineation of the educational gaps that exist for frontline healthcare providers (HCPs) in the realms of recognition, diagnosis, and management of AKI is not well studied.
Methods: Multinational, multi-disciplinary survey conducted between August and September 2020 including 1006 HCPs comprised of emergency medicine (ED), internal medicine/hospitalist (IM), cardiology (CV), nephrology (NEPH) and intensive care (ICU) providers from 6 developed nations in Europe and North America. Respondents were voluntary and recruited from an existing database of HCPs (all HCPs had >70% time as clinical effort and had a minimum 2-year experience) and were reimbursed for participation in the survey.
Results: 98% of surveyed HCPs felt AKI was associated with increased morbidity but less than half (41%) followed existing KDIGO AKI guidelines for the detection and/or management, or treatment of AKI - this varied across discipline, NEPH (72%) vs. IM and ICU (40 and 47%, respectively), ED and CV (19 and 29%, respectively). 72% of surveyed HCPs (n= (724) state there is some delay in diagnosing AKI in their hospital and 95% (n=956) state that the not recognizing AKI early can have a significant financial impact to the healthcare system. Further analyses revealed 53% of surveyed HCPs (n=538) simultaneously indicated AKI increases both morbidity and mortality yet current methods of diagnosis mean AKI is often missed (ICU and NEPH – 66 and 62% versus internists and ED HCPs (42 and 39%). While 69% of surveyed HCPs (n=695) believed changes in creatinine and/ or urine output were not sensitive nor specific for AKI, 45% believed improved diagnostic methods and tools would help improve early AKI detection (including biomarkers, more frequent diagnostics). In a stepwise analysis of sequential questions, HCPs demonstrated a differential response (Figure 1). 91% of surveyed HCPs indicated a strong need for further medical education on AKI for all clinical wards.
Conclusion: In a survey of AKI care providers across various disciplines, appreciation that AKI associates with negative outcome is nearly universal, however opportunities

for education were identified. HCPs frequently indicated a desire to improve diagnostic accuracy and reduce missed AKI diagnoses, and also reported inconsistent adherence to AKI guidelines. Analysis of of HCPs may help improve the precision of AKI educational efforts.

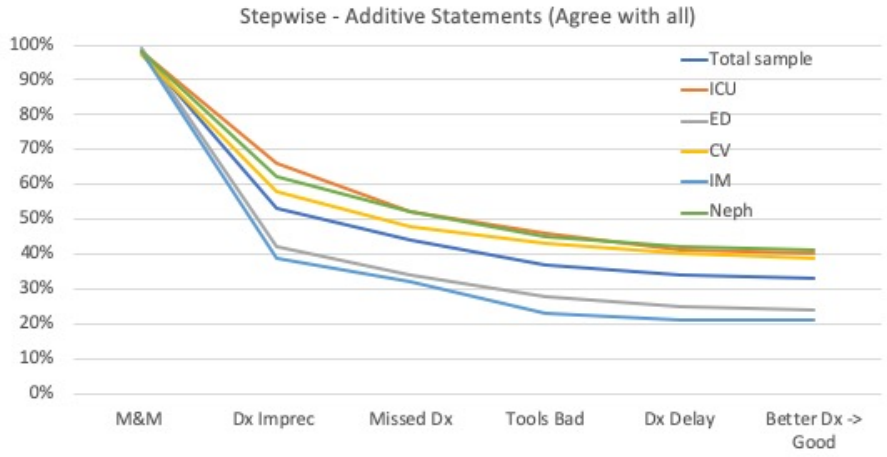

Figure 1. Physicians who believe improved diagnostics can improve outcome.
A cumulative, question-by-question agreement showing the proportion of subspecialty field in agreement for sequential questions of: 1) if AKI increases morbidity and mortality (M&M), 2) if current diagnostics are imprecise (Dx Imprec), 3) if AKI diagnosis is missed, 4) AKI diagnostics are nonfunctional (Tools Bad), 5) if poor diagnostics lead to delayed care, 6) and if improved diagnostics can ultimately improve patient outcomes.
(ICU-intensive care, ED-emergency medicine, CV-cardiology, IM-internal medicine, NEPH – nephrology)

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Derivation and validation of a modified renal angina index to predict poor outcomes after pediatric heart surgery

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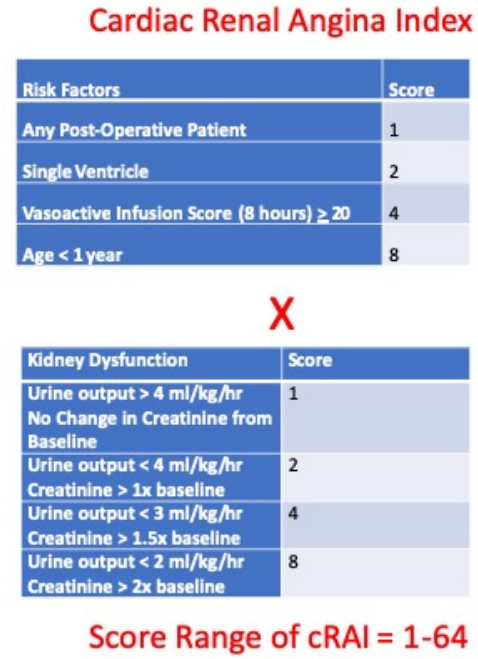
Purpose: Identification of patients following cardiopulmonary bypass (CPB) at risk of complex intensive care unit (ICU) outcome directly and indirectly related to acute kidney injury (AKI) may be important for bedside providers in the immediate post-operative period. We sought to modify the renal angina index, an AKI risk prediction prodrome, for use in children following CPB.

Methods: Multicenter, retrospective study of pediatric patients following cardiac surgery. The cardiac renal angina index (cRAI) was used to score patients at 8 hours following ICU admission from CPB for the fulfillment of cardiac renal angina (cRA+). The cRAI was comprised of risk factors for injury and kidney dysfunction assessed at 8 hours following CPB. The outcome of interest was ICU Complexity as defined by Day 3 AKI, mechanical ventilation duration > 7 days, ICU LOS > 14 days, or death. The optimal cut-off value and performance of the cRAI for prediction of complex ICU outcome was determined via a derivation sensitivity analysis and then a validation analysis.

Results: 597 patients (59% male, age 191 days (IQR:38, 1580 days) were studied. Complex outcome occurred in 168 (28.1%). The sensitivity analysis of the cRAI in the derivation cohort (n=298) is shown in Table 2. The optimal cut-point was determined to be above 8 (cRAI scale of 1-64) and when studied in the validation cohort (n=299), the fulfillment of cRA (using cRAI>8) demonstrated a specificity , sensitivity, and negative predictive value of for complex outcome. The receiver operating characteristic of the cRAI (n=597) was 0.70 (0.62-0.75).

Conclusion: The modified renal angina index can be used to predict complex outcome in children following cardiopulmonary bypass. Further revision and modifications of the construct may be required in analysis in larger population samples, however, the

fulfillment of renal angina in the cardiac population can be determined shortly after CPB to help with longer term ICU prognosis in children following cardiac surgery.



Metric	Sens	Spec	PPV	NPV	Youden's
ALL	100 (96-100)	0	28 (28-28)	0	0
cRAI >1	96 (90-99)	14 (10-19)	30 (29-32)	91 (76-97)	10.3
cRAI >2	95 (88-99)	18 (13-24)	31 (29-33)	91 (78-96)	13.3
cRAI >4	89 (80-95)	25 (19-31)	32 (29-34)	86 (76-92)	14.3
cRAI >8	63 (51-73)	73 (66-78)	47 (40-54)	83 (79-87)	35.2
cRAI > 16	56 (45-67)	78 (72-83)	50 (42-58)	83 (78-86)	34.8
cRAI > 32	31 (22-42)	88 (83-92)	50 (38-62)	77 (74-79)	19.2
Single Ventricle	46 (35-57)	87 (81-91)	57 (47-67)	80 (77-83)	32.3
VIS8>20	42 (31-54)	87 (82-91)	56 (45-66)	79 (76-82)	29.1
Age < 1y	83 (73-91)	51 (44-58)	40 (36-44)	89 (83-93)	34.3
UOP < 4	66 (55-76)	41 (34-48)	20 (27-35)	76 (69-81)	7.1
UOP < 3	35 (25-46)	62 (55-68)	26 (20-33)	71 (67-75)	9.1
UOP < 2	63 (51-73)	73 (66-78)	47 (40-54)	83 (79-87)	-3.2

The performance of the cRAI (cardiac renal angina index) as it varies from 1-64 is shown above compared to single ventricle anatomy, a vasoactive infusion score (VIS) at 8 hours of ≥20, and age under 1 year (risk factors in cRAI) and urine output (UOP) under 2, 3, and 4 ml/kg/hr (injury factors in cRAI). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are shown with 95% confidence intervals.

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Urinary Neutrophil Gelatinase Associated Lipocalin for Phenotyping Acute Kidney Injury in the Setting of SARS-CoV2

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Background and Objectives: In the available data, children with SARS-CoV2 infection are at risk for acute kidney injury (AKI). The severity of AKI in these children has yet to be characterized and may be dependent on the type of SARS-CoV2 infection. Urinary AKI biomarkers such as neutrophil gelatinase associated lipocalin (uNGAL) may be helpful in phenotyping AKI in the context of critical illness.

Design, Setting, Participants and Measurements: We conducted a single-center prospective observational study of children admitted to the intensive care unit (ICU) with concerns for SARS-CoV2. Patients were tested for virus using polymerase chain reaction (PCR) and antibody testing (Ab). On admission to ICU, uNGAL was assessed in patients able to void urine spontaneously or with an indwelling catheter. AKI stage (using KDIGO creatinine-based staging) was assessed during ICU course. SARS-CoV2 exposure was cohorted by result of PCR and Ab testing.
Results: 16 children were studied in the first 5 months of the pandemic (Male 10 (62.5%), age 13 (5, 17.5), 14 were discharged home from the ICU and 2 died. Results from the patients are shown in Table 1. AKI was prevalent in children tested (15, 93.8%) with 4 (25%) having severe AKI at time of uNGAL assessment. All patients positive for both PCR and Ab (n=6) had an increase in AKI severity after uNGAL assessment. Patients positive for Ab only demonstrated a decrease in AKI severity from time of uNGAL while patients positive for PCR only demonstrated an increase in AKI severity from time of uNGAL.
Conclusions: In this interim analysis, uNGAL testing in a small sample of critically ill children suspected of having SARS-CoV2 exposure demonstrates ability to delineate transient AKI from persistent AKI early in ICU course. Patients with SARS-CoV2 positive exposure by PCR testing have progressive AKI severity compared to SARS-CoV2 positive exposure by Ab testing, indicative of the AKI associated with COVID-19 versus multi-inflammatory syndrome in children (MIS-C), respectively. Given the emerging knowledge about AKI severity in adults and children, and the strain on available resources, early triage of AKI may be useful for triage of critical care support. Expanded study of our preliminary results is warranted.

Patient Age (Years)	Patient Gender	SARS-CoV2 Ab	SARS-CoV2 PCR	uNGAL on ICU Admit	Baseline SCr	SCr on ICU Admit	Max SCr in ICU	ICU Stage on ICU Admit	Max ICU Stage in ICU
21	Male	Negative	Negative	15	1.45	1.55	2.02	1	1
1	Male	Negative	Negative	14	0.30	0.27	0.27	0	0
11	Female	Negative	Positive	594.3	0.43	0.55	0.71	1	1
0.5	Male	Negative	Positive	72	0.38	0.44	0.54	1	1
15	Male	Negative	Positive	383	0.37	0.44	0.51	1	1
9	Female	Positive	Negative	38	0.5	0.56	0.56	1	1
6	Female	Positive	Negative	32	0.35	0.44	0.44	1	1
15	Female	Positive	Negative	73	0.45	0.89	0.89	2	1
5	Male	Positive	Negative	46	0.36	0.42	0.46	1	1

20	Female	Positive	Positive	280	1.1	1.9	1.9	1	2
5	Male	Positive	Positive	1137	0.31	2.44	3.21	3	3
17	Male	Positive	Positive	5	0.83	1.17	1.17	1	1
17	Male	Positive	Positive	2917	0.45	2.92	5.15	1	2
18	Female	Positive	Positive	57	0.38	0.48	0.61	1	1

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Developing An Acute Peritoneal Dialysis Program In Response To COVID-19 Pandemic

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IntroductionThe coronavirus disease of 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), continues to spread around the world. Acute kidney injury (AKI) is one of the most serious complications of COVID-19 and a major determinant of resource utilization especially if renal replacement therapy (RRT) is needed. Accumulating data suggests that in a subset of patients, peritoneal dialysis (PD) can be an appropriate alternative to conventional RRT modalities used in the acute setting. Herein, several key requirements for setting up an interdisciplinary acute PD program for patients with COVID-19 (APD-COVID) are described.Methods:The 2 main components needed for APD-COVID are: 1) Facilities: A hospital with the ability to provide care for COVID-19, and an affiliated conventional PD program, 2) Personnel: the APD-COVID team is composed of a nephrologist (with experience in PD), an intensivist or pulmonary specialist, and a PD access specialist (an interventional nephrologist/radiologist or a dedicated surgeon with expertise in PD catheter placement and availability for management of catheter-related complications). A PD nurse and a social worker are also part of the team. Results:Convincing data has emerged on the role of APD in successful management of AKI in a subset of patients with COVID-19. An interdisciplinary approach would ensure appropriate patient selection, efficient communication, and optimal timing of initiation of therapy. Accumulating data supports feasibility and safety of percutaneous implantation at bedside, which is of utmost importance in critically-ill population. APD-specific regimens and protocols (e.g. continuous, cycler-assisted, incremental dose) should be implemented based on an individualâ�?��?�s clinical needs e.g. efficient water/ sodium extraction and waste products removal. More advanced objective monitoring methods of volume status (e.g. point-of care ultrasound) could prove useful. Conclusion:Shortages in supplies, staffing, and available equipment have demanded implementation of alternative strategies such as APD for treatment for AKI in critically-ill patients with COVID-19. In a progressive

model of flexible patient-centric healthcare system, setting up an interdisciplinary APD-COVID is both desirable and feasible. Not only will it counter the unprecedented strain on resources, but it also helps with the safe transition to in-home therapy should the need for RRT continue after discharge

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CITRATE PHARMACOKINETCS IN ACUTE LIVER FAILURE CRITICALLY ILL PATIENTS RECEIVING CONTINUOUS RENAL REPLACEMENT THERAPY

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Background: Citrate metabolism was theoretically incomplete in acute liver failure (ALF) patients who require continuous renal replacement therapy (CRRT) support with regional citrate anticoagulation (RCA). However, the pharmacokinetics and metabolism of citrate in these specific settings do not fully understand.

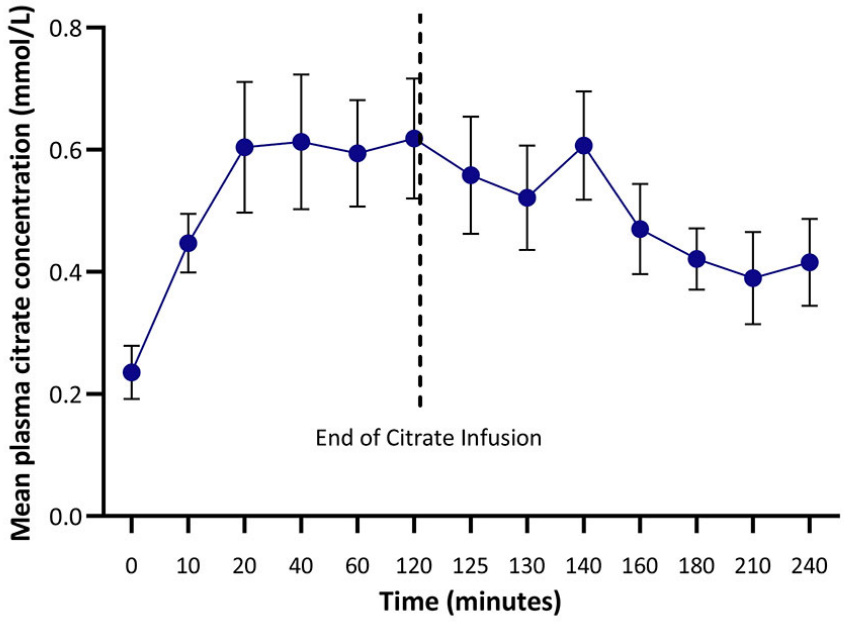
Objective: This study aims to evaluate citrate pharmacokinetics among acute liver failure critically ill patients receiving CRTT.

Methods: This prospective pharmacokinetic study was conducted at King Chulalongkorn Memorial Hospital between July 2019 to October 2020. Seven ALF patients who received CRRT support used isotonic citrate solution as an anticoagulant. We targeted the citrate dose at 3 mmol/L. The citrate toxicity was monitored by using the ratio of systemic total calcium and free ionized calcium ratio every 1 hours. For citrate pharmacokinetics evaluation, we delivered citrate for 120 minutes and stopped for 120 minutes. The body citrate clearance was defined as subtracting of total citrate clearance by filter clearance. Pharmacokinetic parameters were performed via noncompartmental analysis using Phoenix® WinNonlin ®.

Results:
Of note, 7 ALF patients were enrolled. The mean serum total bilirubin was 19.5±8.9 mg/dL, the mean direct bilirubin was 13.1±6.4 mg/dL, the median AST was 760 (191-808) U/L and the median ALT was 567 (125-813) U/L. Total body clearance of citrate in acute liver failure was 152.5±50.9 mL/min which decreased by 50% compared to cirrhosis patients (340±185 mL/min) and 75% compared to healthy patients (686.6±353.6 mL/min) in the previous study. Citrate peak concentrations and concentration over time were increased by 0.76±0.27 mmol/L and 267.2±111.7 mmol.min/L, respectively. There was one patient with serum total calcium to ionized calcium ratio > 2.5, but there was no metabolic acidosis in this patient. Symptomatic or severe hypocalcemia was not found in our study.

Conclusions:
Citrate clearance was significantly decreased in critically ill patients with acute liver failure receiving CRRT. Citrate use as anticoagulation in these subgroup patients should be used with caution.

Figure: Plasma Citrate concentration in critically ill patients with AKI with acute liver failure



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Acid-base alterations associated with PLEX in patients with COVID-19

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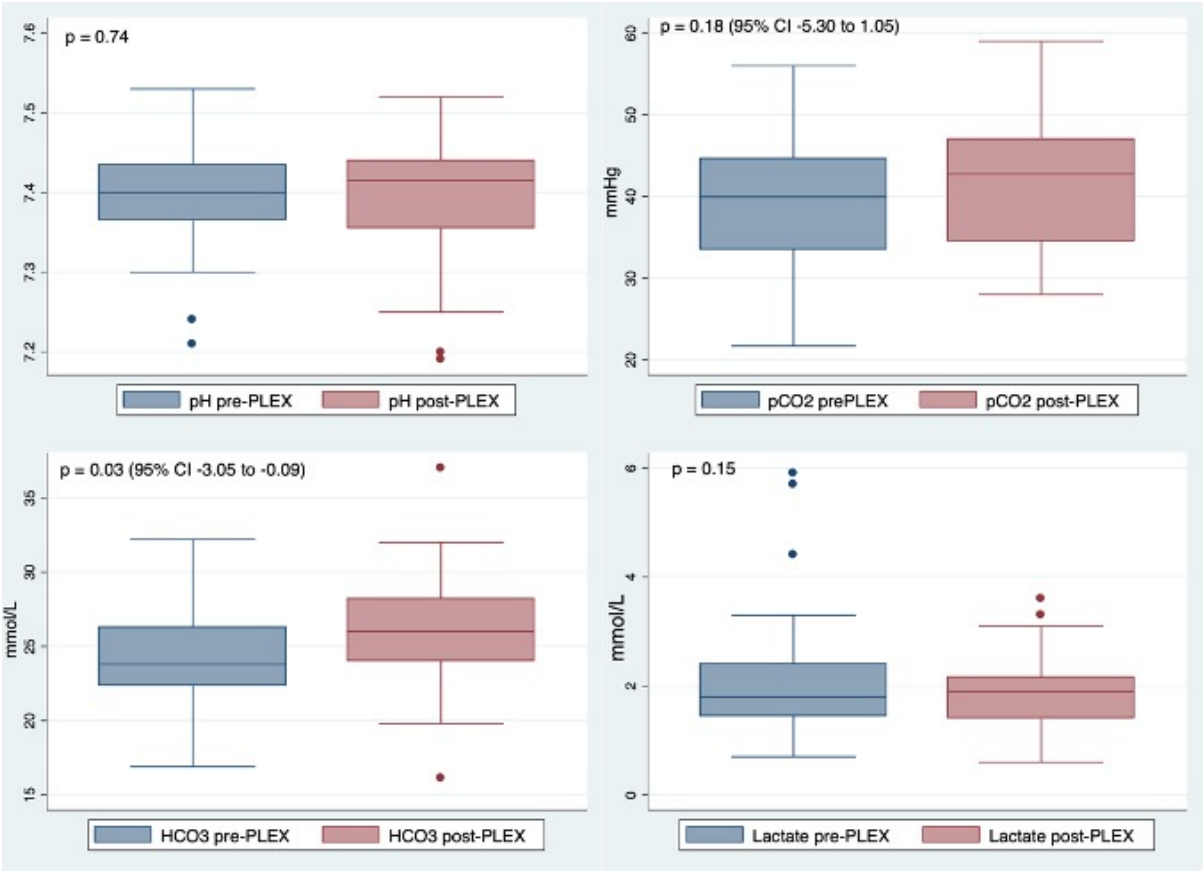
**Centro Médico Nacional "20 de Noviembre"*

Introduction: Complications with the new coronavirus disease are due to the development of a "cytokine storm." These complications include acute respiratory distress syndrome (SARS-CoV-2). Emerging data point to the rationale for using extracorporeal therapy to normalize cytokine levels and reduce the severity of the organic condition. Therapeutic plasma exchange (PLEX) has inherent risks of adverse effects including acid-base disturbances which can complicate the underlying disease state. Albumin, as it has a negative charge, acts as a weak non-volatile acid, so its reduction by 1 gr / dl can increase bicarbonate levels by 3.4 mmol/L. Therefore, hypoalbuminemia can generate alterations in the acid-base balance due to its alkalizing effect.
Material and methods: The results of 40 sessions of PLEX with 3% albumin substitution fluid were evaluated, the pre-PLEX vs post-PLEX figures of the variables pH, CO2, HCO3, lactate and albumin were compared. The variables were compared with the Wilcoxon rank test or T-student test depending on the normality distribution of the variables. A p value <0.05 was considered statistically significant.
Results: 40 sessions of plasma exchange (PLEX) were performed in patients with COVID-19 in our center, from May to October 2020. Arterial gases were obtained, obtaining the following values (pre-PLEX vs 24 hs post-PLEX): pH (7.39 ± 0.06 vs 7.39 ± 0.07; p = 0.74); HCO3 (24.39 ± 3.39 mmol / L vs 25.96 ± 3.83 mmol / L; p = 0.03, 95% CI -3.05 to -0.09); CO2 (39.71 ± 7.63 vs 41.8 ± 8.80 mmHg; p = 0.18, 95% CI -5.30 to 1.05); lactate (2.10 ± 1.10 vs 1.84 ± 0.66; p = 0.15); albumin (3.20 ± 0.40 vs 3.21 ± 0.56; p = 0.66).
Discussion: A significant difference was found in the pre-PLEX vs post-PLEX plasma HCO3 value, although the albumin values were not different between the samples, nor did it seem to be related to previous hypercapnia given the pre-PLEX pCO2 concentration. According to the studies of Fencl et al, and in agreement with the Stewart model, the hypoalbuminemia present during the course of therapy explains the generation of metabolic alkalosis due to the reduction of a primary element of ATOT (non-volatile weak acids).
Conclusion: It was found that the predominant acid-base disorder associated with PLEX was metabolic alkalosis, associated with hypoalbuminemia, which is not

related to therapy but probably to the redistribution of serum albumin from the intravascular compartment and / or due to the acute inflammatory state.



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The structure of hemodialysis catheter may alter the actual blood flow rate in hemodialysis therapy in vitro

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Background
Hemodialysis catheters are widely used in patients requiring continuous renal replacement therapies for obtaining adequate vascular access. Despite the recent improvements in the catheter structure, the type of catheter that are adequately efficient at a high blood flow remain obscure.

Purpose
To compare the actual blood flow rate of various types of hemodialysis catheter available on the application of a flow rate.

Methods
The blood purification machine DBG-03 and the blood circuit were employed. Three different types of catheters (e.g., Flexxicon II, Niagara Slim and Niagara Slim with side holes) were connected to the blood circuit. About the arterial tip structure of the catheter, Flexxicon II has 8 side holes, Niagara Slim has only one end hole, Niagara Slim with side hole has two side holes and one end hole. An in vitro evaluation system was developed for this study. Each catheter was inserted into a 50% glycerol solution and the arterial joint was connected to the arterial blood circuit. On the other hand, the vein blood circuit was connected to another same type of the vein joint. The circuit was filled with 50% glycerol solution, at a blood flow rate of 100 - 300 mL/min. The actual blood flow was estimated with measuring cylinder at the outflow on the venous side. The actual blood flow of these each catheter were then compared.

Results
When the predicted flow rate was 100 mL/min, Flexxicon II showed 95.0 ± 0.56 mL/min, Niagara Slim showed 97.0 ± 1.20 mL/min and Niagara Slim with side holes showed 97.0 ± 1.07 mL/min. When the predicted flow rate was 300 mL/min, Flexxicon II showed 219.6 ± 0.01 mL/min, Niagara Slim showed 265.9 ± 0.01 mL/min and Niagara Slim with side holes showed 263.9 ± 0.70 mL/min.

Conclusions
The present data suggest that when a high blood flow is required, the type of hemodialysis catheter required is determined based on their characteristics.

RRT APPLICATIONS AND TARGETED INTERVENTION

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Severe Methanol Poisoning Treated with the Tablo Hemodialysis System: A Case Report and Analysis

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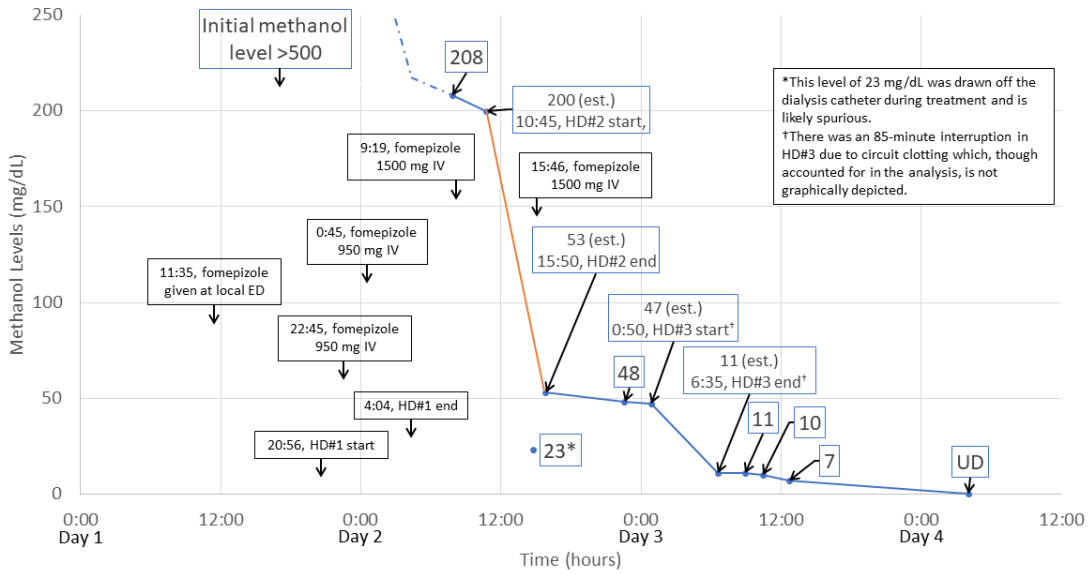
Case
A 100-kg 36-year-old man was found down with depressed mental status and taken to a local hospital, where labs reportedly included undetectable blood ethanol and an anion gap >40. He was intubated for airway protection, given fomepizole, and transferred to our facility. Initial labs included a persistent anion gap metabolic acidosis and osmolar gap of >200 mOsm/kg. Hemodialysis (HD) access was placed, additional fomepizole was given, and a toxic alcohol panel was drawn which ultimately revealed a methanol (MeOH) level >500 mg/dL. He received 3 total HD sessions, the first 2 with the Tablo System (Outset Medical) and the 3rd with a conventional HD machine (Gambro Phoenix, Baxter). All 3 utilized a Revaclear dialyzer [Baxter, KoA for urea of 1,170 mL/min at blood flow 300 mL/min and dialysate flow (Qd) 500 mL/min]. See Figure for treatment sequence and serial MeOH levels. With HD the patient recovered from his poisoning, though he did experience significant persistent visual impairment.

Analysis
MeOH has unicompartmental kinetics, with no rebound in levels after HD. Using published pharmacokinetic data for MeOH (including conservative values for an endogenous half-life of 52h in the setting of alcohol dehydrogenase inhibition and a volume of distribution of 0.6 L/kg), we undertook a formal regression analysis of the available MeOH levels in logarithmic space to estimate MeOH clearance during the 2nd and 3rd HD sessions, yielding clearances of 239 mL/min (95% CI 173-305) for Tablo and 341 mL/min (95% CI 252-429) for conventional HD. Both are within the range of clearances achieved with HD previously reported in the literature of 77-400

(mean 208) mL/min.

Discussion

This case was part of an outbreak of MeOH poisoning in May and June 2020 in the southwest U.S. linked to ingestion of contaminated hand sanitizer imported during the COVID-19 pandemic which resulted in 15 admits and 4 deaths. Tablo is a novel HD system with incorporated reverse osmosis system, allowing for increased portability and simplified sterilization, which led our facility to adopt Tablo as our default portable HD device during our COVID-19 surge. This is the first reported case of the use of Tablo to treat toxic alcohol poisoning. Despite a being limited to a maximal Qd of 300 mL/min, this case illustrates that HD with Tablo can achieve a clearance of MeOH well within the previously published standard of care, a clearance that could be enhanced further with a high KoA dialyzer.



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Retrospective Analysis Comparing Complication Rates of Centrifuge vs Membrane-based Therapeutic Plasma Exchange

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Background: There are two conventional modalities used to perform Therapeutic Plasma Exchange (TPE): centrifuge TPE or membrane-based TPE. The efficacy of both has been described; however, there is limited data on patient and circuit complications with membrane-based TPE. As opposed to centrifuge TPE, membrane-based TPE commonly uses heparin as it is a simpler approach to anticoagulation.

Objective: We sought to better understand the patient and circuit complications of membrane-based TPE and compare them to centrifuge TPE. We hypothesize that our membrane-based TPE protocol is both safe and effective.

Methods: We retrospectively evaluated patients 21 years of age and younger who required TPE from 2012 through 2019 from our TPE Quality Improvement database. Patients who underwent TPE and Extracorporeal Membrane Oxygenation (ECMO) in tandem were excluded. Patient and machine complication rates were compared between the patients who received centrifuge TPE (with citrate anti-coagulation) and membrane-based TPE (with heparin).

Results: Of the 105 patients who met inclusion/exclusion criteria, 63 received centrifuge TPE via Optia and 42 membrane-based TPE via Prismaflex. Those who used membrane-based TPE were younger (4.82 ± 2.82 years vs 15.24 ± 3.73 years, p value 0.0001) and weighed less (19.48 ± 10.55 kg vs 71.72 ± 28.46 kg, p value 0.0001). There were no significant differences in patient-related complications or indications for TPE between the two modalities. Of the 1031 procedures, 5 were excluded as they did not use any anticoagulation and 28 were excluded for citrate anticoagulation on membrane TPE; thus, 646 treatments using centrifuge TPE were compared to 357 using membrane-based TPE. There was no significant difference in rates of abnormal calcium levels or patient-related complications between groups. More membrane-based TPE procedures used albumin replacement ($p< 0.001$). The rates of machine related complications were similar for fever, hypertension/ hypotension, low ionized calcium, allergic reaction and others. More circuits clotted during membrane/heparin based therapies (6.7%) vs (0%); $p<0.001$.

Conclusion: This study shows that even though the membrane-based TPE protocol is used in smaller children it is not associated with higher rates of patient-related complications in comparison to centrifuge TPE. Although the overall rate of circuit clotting using membrane TPE was low, it occurred more commonly than with citrate TPE.

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Idiopathic Hyperammonemia Post PBSCT Requiring RRT

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Idiopathic Hyperammonemia is defined as elevated serum ammonia levels in the absence of abnormal liver function tests. It has been associated with high dose chemotherapy and post stem cell transplant in patients with hematological malignancies.
42-year-old African American male with past medical history of Acute Lymphocytic Leukemia diagnosed in June 2019 admitted to hospital for Matched unrelated Peripheral Stem cell transplant. Induction therapy was done with anti-Thymoglobulin, cyclophosphamide and total body irradiation. Post-transplant hospital stay was complicated by neutropenic fever, E. coli colitis, multi-focal pneumonia, and coagulase negative bacteremia. He had received multiple antibiotics throughout his hospital stay. He has also been on tacrolimus with high tacrolimus levels. Nephrology was consulted for the management of acute kidney injury. Patient had been non-oliguric throughout the admission. His serum creatinine increased from baseline of 0.8mg/dL to a peak of 4.0mg/dL. Patient had been tachypneic and tachycardic for several days with worsening of his SOB, and was eventually transferred to Medical Intensive Care Unit, where he was intubated. He was also hypotensive and started on Nor-epinephrine. His serum ammonia 1-day prior was 87 mcmol/L. His CT brain was negative for any acute abnormalities. Patient started to have refractory seizures the next day and had to be paralyzed. CT brain showed subtle blurring of the gray-white matter differentiation. Patient was started on CVVH for uremic encephalopathy and refractory seizures as patient was on multiple medications that lowered seizure

threshold. His ammonia level came back at 870 mcmol/L. Repeat CT scan next day showed worsening of cerebral edema and ammonia levels of 1070 mcmol/L. BUN had decreased appropriately by 30% in 24 hours. CVVH was held as EEG changes consistent with cerebral edema were coincident with initiation of RRT. Patient's ammonia continued to rise. His liver function tests were normal throughout the hospitalization. Eventually CVVH was resumed but his ammonia continued to rise (peaking at 1500 mcmol/L) despite RRT and patient passed.
Idiopathic Hyperammonemia is a serious complication which can result in rapid deterioration of mental status, seizures, coma and death. Early recognition and treatment is important as it can be fatal. It is also important to study the mode of RRT in these patients to effectively and safely remove ammonia.

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Continuous Kidney Replacement Therapy During Pandemic Era: Experience of Two Cases in Pediatric Chronic Kidney Disease Patients

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Background:
During the SARS-CoV-2 pandemic era, high incidence of infection and low test rate in a developing country is extremely hazardous for chronic kidney disease (CKD) children. Poor immune system and immunosuppressive medications in CKD children increase the risk of infection, including SARS-CoV-2, also increase the disease severity and mortality. When hemodynamically unstable, (continous kidney replacement therapy) CKRT is preferable. The challenges to deliver effective CKRT during pandemic in two cases of pediatric CKD patients were reported in our study .
Cases:
The first case, a 17 years-old boy with focal segmental glomerulosclerosis, end-stage kidney disease with routine hemodialysis therapy, and renal anemia. He had hospitalized for steroid pulse therapy and received packed red cell (PRC) transfusion for anemia. Afterwards, he developed fever and respiratory distress. Since respiratory distress had worsen in less than 24 hours, he was intubated and started for lung recruitment for acute respiratory distress syndrome (ARDS) in (pediatric intensive

care unit) PICU. Later he was evident with acute on CKD, unstable hemodynamic and needed for fluid removal to support management in ARDS. CKRT was initiated from day-3 until day-5 of PICU admission. After CKRT, the respiratory symptoms and radiologic features improved. Nevertheless, we found negative results for reverse transcriptase-polymerase chain reaction (RT-PCR) SARS-CoV-2, but positive result for anti-SARS-CoV-2 IgG at day-10 from the first symptoms.
The second case, a 15 years-old girl with lupus nephritis class III, acute on CKD, and COVID-19 ARDS. She came to the hospital with dyspnea and fever. She was intubated on day-2 and started for lung recruitment due to worsen respiratory condition in PICU. She developed edema and decreased urinary output. She had fluid restriction, furosemide continuous infusion and correction for hypoalbuminemia. CKRT was initiated on day-4 of admission. During CKRT, respiratory and hemodynamic problems were more profound and she passed away on day-5. RT-PCR test for SARS-CoV-2 from nasopharyngeal swab confirmed positive results.
Conclusion:
In pediatric acute on CKD patients with hemodynamic instability and ARDS, CKRT plays a role to support comprehensive management in PICU.

Parameters	1st Case	2nd Case
1. Clinical parameters	71	55
Onset for respiratory distress	1 day	3 day
Heart ejection fraction baseline	69%	77%
PaO2/FiO2 ratio	58.8	53.2
Oxygen index at time of lung recruitment	30.1	43
Urine output (mL/kg/hour)	0	<0.5
2. Biochemical parameters		
CRP (ng/mL)		
Pre-CKRT	287	18.8
Post-CKRT	NA	NA
Procalcitonine (ng/mL)		
Pre-CKRT	101.6	0.32
Post-CKRT	NA	NA
eGFR (mL/minute/1.73m2)		
pre-admission	6	58.6
Pre-CKRT	2	33.5
Post-CKRT	19.2	39.8

Calcium ion (mmol/L)		
Pre-CKRT	0.96	0.98
Post-CKRT	1.01	1.3
Phosphate (mg/dL)		
Pre-CKRT	10	7.6
Post-CKRT	4.8	NA
3. Supportive management		
Lung recruitment	yes	yes
Steroid for ARDS	yes	no
Inotrope support	no	yes
1 inotrope	no	no
≧ 2 inotropes	no	yes
4. CKRT setting		
Anticoagulation	heparin	heparin
Dialyzer	M100	M100
Blood (ml/min)	220	220
Pre blood pump (ml/h)	0	500
Dialysate (ml/h)	850	700
Replacement (ml/kg/h)	1200	800
Patient fluid removal (ml/h)	50	30
Effluent dose (ml/kg/h)	30	37
Ultrafiltration dose (ml/kg/h)	16	23
Filtration fraction (%)	13	13
Filter age (hours)	65	20

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Successful Extracorporeal Organ Support (ECOS) Therapy In COVID-19 Pneumonia: A Case Report.

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**Christus Muguerza Alta Especialidad, Monterrey, Nuevo León, México*

Patients with severe COVID-19 pneumonia can develop acute respiratory distress syndrome, which triggers respiratory failure. Extracorporeal organ support therapies (ECMO, CRRT, plasmapheresis) can be used as part of adjunctive management in patients with refractory hypoxemia even with the appropriate use of optimal mechanical ventilation (IMV) and pharmacological measures. We describe a case of a 31-year-old man with a history of morbid obesity admitted for respiratory failure due to Covid-19 pneumonia. Upon admission, he is managed with mechanical ventilation and because his poor evolution and hypoxemia; it was decided to start ECMO therapy within the first 24 hours of admission; subsequently, management with CRRT with prismaflex and oXiris filter with CVVHDF modality is initiated in the second day of hospitalization. One day later, treatment with plasmapheresis is also applied. The patient presents a rapid clinical improvement and a significant decrease in inflammatory markers so it was decided to withdraw ECMO and CRRT on the fourth day of admission, and VMI 24 hours later. The clinical deterioration of patients with COVID-19 is believed to be a result of an inflammatory state caused by a cytokine storm. CRRT with oXiris filter has been associated with a significant reduction in cytokine and endotoxin levels thanks to its extracorporeal purification capacity; it is being used for hemofiltration due to the high capacity to adsorb endotoxins and cytokines. On the other hand, plasmapheresis treatment also eliminates inflammatory mediators by replacing plasma containing these molecules with albumin. Management with ECMO has shown benefits as a salvage therapy in patients with severe hypoxemia despite use of IMV. The success of these treatments depends largely on the early onset of ECOS in the critically ill patient. Starting them at the most opportune time, as in our case, is key to the patient's clinical improvement.

	IMV	IMV ECMO	IMV ECMO CRRT	IMV ECMO CRRT Plasmapheresis	IMV Plasmapheresis	Plasmapheresis
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Hemoglobin (g/dL)	14.3	13.7	11.4	10.1	-	9.6
Leukocytes (K/μL)	8.52	10.09	5.88	9.16	-	10.64
Lymphocytes (K/uL)	0.44	0.56	0.57	0.60	-	1.01
Creatinine (mg/dL)	0.82	0.83	3.01	2.59	1.08	1.29
BUN (mg/dL)	11.8	16	43.9	40.7	17.7	21.7
Alkaline phosphatase (U/L)	94	85	60	52	-	26
LDH (U/L)	903	1126	1087	897	-	487
C-reactive protein (mg/L)	207.36	205.65	-	57.3	-	-
Interleukin 6 (pg/mL)	-	-	-	505.7	167.5	177

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The Successful Use of Prolonged Intermittent Renal Replacement Therapy In Pediatric Heart Transplant Recipients in the Cardiovascular Intensive Care Unit

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Background: Continuous Renal Replacement Therapy (CRRT) is known to be the preferred method of dialysis in critically ill patients unable to tolerate intermittent hemodialysis (IHD). CRRT, however has limitations with mobility and greatly inhibits physical and occupational therapy sessions. The use of prolonged intermittent renal replacement therapy (PIRRT) has been well described in the adult population, however there is limited evidence for the use of PIRRT in pediatric patients.

Methods: A retrospective cohort study was performed and identified three pediatric heart transplant recipients aged 14-18 years in the cardiovascular intensive care unit (CVICU) who underwent PIRRT. Demographics included a) CRRT requirement for more than 28 days, b) hemodynamically unstable to undergo IHD c) deemed to have severe deconditioning by the physical therapist, and d) extubated and alert. PIRRT was initiated at 20 hours and progressively increased until the subjects were able to safely transition to IHD.

Results: PIRRT was successful in 100% of patients with no reported adverse events. This allowed the subjects to participate in our facility's intensive physical therapy program during the day and achieve clearance and volume removal in the evenings. Due to the allowance of intense physical therapy and improvement in muscle strength, these patients did not require transfer to an inpatient rehabilitation facility. 100% of the patients were successfully transitioned to an outpatient IHD clinic upon discharge.

Conclusions: The use of PIRRT in this pediatric heart transplant population played a vital role in their physical rehabilitation course. The hours off CRRT allowed for improved mobility and a predictable schedule for completing activities of daily living with limited assistance from hospital staff. Further implications of study should include larger sample and population sizes with pediatric patients.

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Clinical Pathway for Peritoneal Dialysis Catheter Placement in the Pediatric Cardiovascular Intensive Care Unit

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Background: Acute kidney injury (AKI) after cardiopulmonary bypass (CPB) is common in neonates and is associated with poor outcomes. Early initiation of dialysis in neonates undergoing cardiac surgery with CPB has proven to be safe and improve outcomes. Understanding which patients would most benefit from intraop placement of PD catheters for early initiation of dialysis is needed to optimize care.

Objective: We sought to determine patient specific characteristics of neonates undergoing cardiac surgery with CPB that place them at risk for development of severe AKI to determine which neonates would most benefit from early PD.

Methods: We retrospectively evaluated neonates with congenital heart disease requiring cardiac surgery with CPB admitted to the CICU from October 2012 through June 2016. Patients were classified as those who “needed PD” and those who “did not need PD.” Those who “needed PD” had a PD catheter placed in the OR that was used for >2 days, or those who did not have a PD catheter placed in the OR, but in retrospect would have benefited from PD based on >10% fluid overload plus one of the following: intubated > 48 hours, open chest > 48 hours and/or ECMO. Those who “did not need PD” did not have a PD catheter placed, or if placed, it was removed or put to drain ≤ 48 hours post-op.

Results: Of the 148 subjects, 45% were categorized as “needing PD” and 55% as “did not need PD.” The sensitivity and specificity for PD catheter placement in the OR and “needed PD” was 86.6% and 49.5%, respectively. Those who "needed PD" were younger on the day of surgery (6.4 [4.5-9.3] days vs 8.3 [5.5-14] days; p value 0.04) and had a lower preop weight (3.1 +/- 0.5 kg vs 3.3 +/- 0.6 kg; p value 0.04). The lowest median preop serum creatinine was equal for both groups (0.5 mg/dL) but differed based on the ranges (IQR 0.4-0.7 vs IQR 0.4-0.6; p value 0.01). Those with an open chest post-op were more likely to need PD (62.7% vs 25.9%; p value <0.001). We determined, serum creatinine ≥ 0.8 mg/dL, pre-op weight ≤ 2.5 kg or open chest post-op will accurately predict the need for PD.

Conclusion: Patient specific characteristics including pre-op weight, pre-op serum creatinine and open chest post-op are associated with neonates “needing PD” post-op. This data has allowed us to adjust our criteria for PD placement to better provide early PD only to neonates who are likely to have a clinical benefit. Additional studies are needed to further validate these findings.

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Prophylactic PD Catheter Placement for Reduction of In-Hospital Mortality in Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass: Systematic Review with Meta-Analysis

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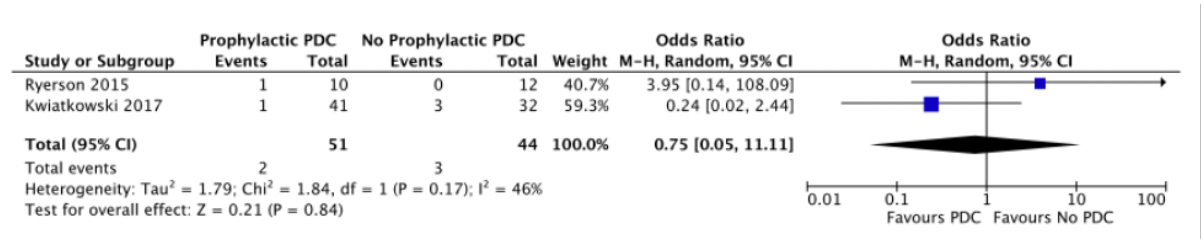
Background: Infants undergoing cardiopulmonary bypass (CPB) are at high risk for acute kidney injury (AKI) and fluid overload, requiring the use of peritoneal dialysis (PD). This systematic review and meta-analysis evaluates whether prophylactic PD catheter (PDC) insertion at the time of cardiac surgery improves outcomes in this population.
Methods: A comprehensive literature search was completed in Oct-2020. Two reviewers independently completed study selection, data extraction, and bias assessment. We identified randomized controlled trials (RCTs) and observational studies (cohort or case-control) from all countries that included children ≤18 years undergoing CPB receiving prophylactic PDC (inserted (1) pre-operatively (but not used) or (2) intra-operatively, or (3) ≤24 hours post-operatively) compared to children who do not undergo prophylactic PDC placement. Outcomes included in-hospital mortality; intensive care and hospital length of stay; presence and degree of fluid overload; time to negative fluid balance; laboratory measures of renal dysfunction; requirement and duration of inotropic support and mechanical ventilation; and presence and severity of PD-related complications. RCTs were evaluated using the Cochrane risk-of-bias; observational studies (including cohort and case-control) were evaluated using Newcastle-Ottawa quality assessment form. Pooled meta-analysis for the outcome of in-hospital mortality was done to show unadjusted odds ratio (OR) with 95% confidence interval (95% CI) using Mantel-Haenszel random-effects model due to the anticipated variability of the populations and interventions studied in RevMan software 9.5. Heterogeneity between studies was assessed using the I2 statistic.
Results: Full-text review of seven articles examining in-hospital mortality were completed for this preliminary analysis. Three studies met inclusion criteria, including two RCTs and one case-control study. The age of infants was 3-15 days. RCTs were found to have high risk for bias, namely due to lack of blinding. The pooled unadjusted OR of in-hospital mortality following cardiac surgery in infants who

underwent prophylactic PDC insertion, relative to those who did not, was 0.75 (95% CI: 0.05-11.11). The meta-analysis showed moderate heterogeneity with I2 value 46%.

Conclusion: The impact of prophylactic PDC insertion in infants undergoing cardiac surgery and/or CPB on reducing in-hospital mortality cannot be determined and requires further study.



NEW TECHNOLOGY

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Single Center Experience: Conversion to Tablo Dialysis System

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Background
St. Mark's Hospital is a 316-bed multi-specialty acute care hospital that converted all dialysis treatments from an outside vendor (OV) to an insourced model using the Tablo Hemodialysis System. Prior to this conversion, the OV provided all dialysis-related equipment, dialysis nurses, and completed the initial setup of CRRT treatments.
Tablo is an easy to learn, compact dialysis machine, capable of providing intermittent and extended therapy treatments. Tablo features integrated water purification, on-demand dialysate production, and includes two-way wireless connectivity allowing for remote monitoring, treatment data transmission and tracking of disinfection schedules in the cloud.
Objective
Single center report on the transition from an outsourced-to-insourced dialysis model using Tablo.
Methods
The initial transition to Tablo occurred in the ICU for SLEDD in April. After training ICU staff and obtaining further experience and familiarity with Tablo, IHD treatments hospital-wide were transitioned in June. Data regarding training, user satisfaction, treatment success, and treatment costs were recorded from 04/20-11/20.
Results
Hospital staff were trained on Tablo after attending a single 4-hour session provided by Outset Medical. A total of 15 ICU nurses, 7 floor nurses, and 3 HD nurses were trained. Post-training survey results were received from 15 respondents, with 80.0% (12) reporting ≤3yrs of dialysis experience. 73.3% (11) rated their overall training experience as Good/Excellent; 80% (12) felt competent performing treatments using Tablo; 73.3% (11) felt comfortable starting a treatment; and 93.3% (13) reported Tablo setup was easier than other RRT machines.

From 04/2020-11/2020, a total of 577 treatments (472 IHD and 105 SLEDD; average treatment time was 200 and 658 minutes, respectively) were performed with a 96.2% success rate. Net savings moving to an insourced model with Tablo are projected at $450,000 in the first year (OV $650,000 vs. Tablo $200,000). Net savings per treatment estimates are $550/treatment (OV $800 vs Tablo $250).
Conclusions
The Tablo Hemodialysis System is an all-in-one dialysis system that can be used across all continuums of nephrology care. Tablo's ease of use allows for the training of existing hospital staff with or without prior dialysis experience. Insourcing of dialysis with the Tablo Hemodialysis System resulted in a high treatment success rate and reduced the overall cost of dialysis delivery.

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Combining Urine Output and intra-abdominal pressure monitoring to predict AKI early

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Introduction/Hypothesis: The incidence of acute kidney injury (AKI) in patients undergoing cardiopulmonary bypass (CPB) is well documented. AKI is associated with increased morbidity, mortality, and healthcare expenditures. In this study, we applied machine learning methods to continuous urinary bladder monitoring of urine output (UO), intraabdominal pressure (IAP) and core temperature (CT) to predict AKI.

Methods: This retrospective observational study analyzed data from 30 adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Demographics, vital signs, and laboratory data were extracted from medical records and continuous UO, IAP and CT from the Accuryn device. Patients with UO KDIGO stage 2 were labeled

(<0.5ml/kg/hr for >12hrs). A machine learning method using gradient boosted tree classifier (AKI Predict) was trained and benchmarked using 3-fold cross validation (train on 2/3s data, validate on remaining 1/3). Specifically, patients were tested hourly using 6hr data windows. Features included a p-norm of minute UO, number of hours in oliguria (UO < 0.5 ml/kg/hr), number of minutes spent in abdominal compartment syndrome pressure levels (ACS) (IAP > 20 mmHg), and median CT. Due to the class imbalance caused by windowing of the data, precision and recall were used to assess performance.

Results: 16 out of 30 patients (median age, 66 [IQR: 60-70] years; 19 [63.3%] male patients) met the criteria for AKI Stage 2. Median CPB pump time and median ICU length of stay across all patients was 2.00 hours and 2.81 days, respectively. Precision and recall were 70.0 +/- 20.9% and 54.1 +/- 20.1%, respectively, for an algorithm capable of detecting AKI 17hrs 3 mins +/- 2hrs 24mins prior to KDIGO criteria. 6 hrs foley catheter data were used to predict stage 2 AKI. Numbers of hours in oliguria and in ACS were the most important predictors of AKI, with relative gain values of 0.359+/-0.147, and 0.275 +/- 0.102 respectively.

Conclusions: Continuous bladder monitoring of IAP, UO and CT enabled prediction of AKI in cardiac surgery patients undergoing CPB. The machine learning algorithm based on these data shows sufficiently high specificity and precision for application in clinical practice but needs to be validated in prospective trials

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Model-Informed Precision Dosing of Vancomycin: External Validation of Vancomycin Population Pharmacokinetic Models in Large Cohorts of Chinese Infected Patients

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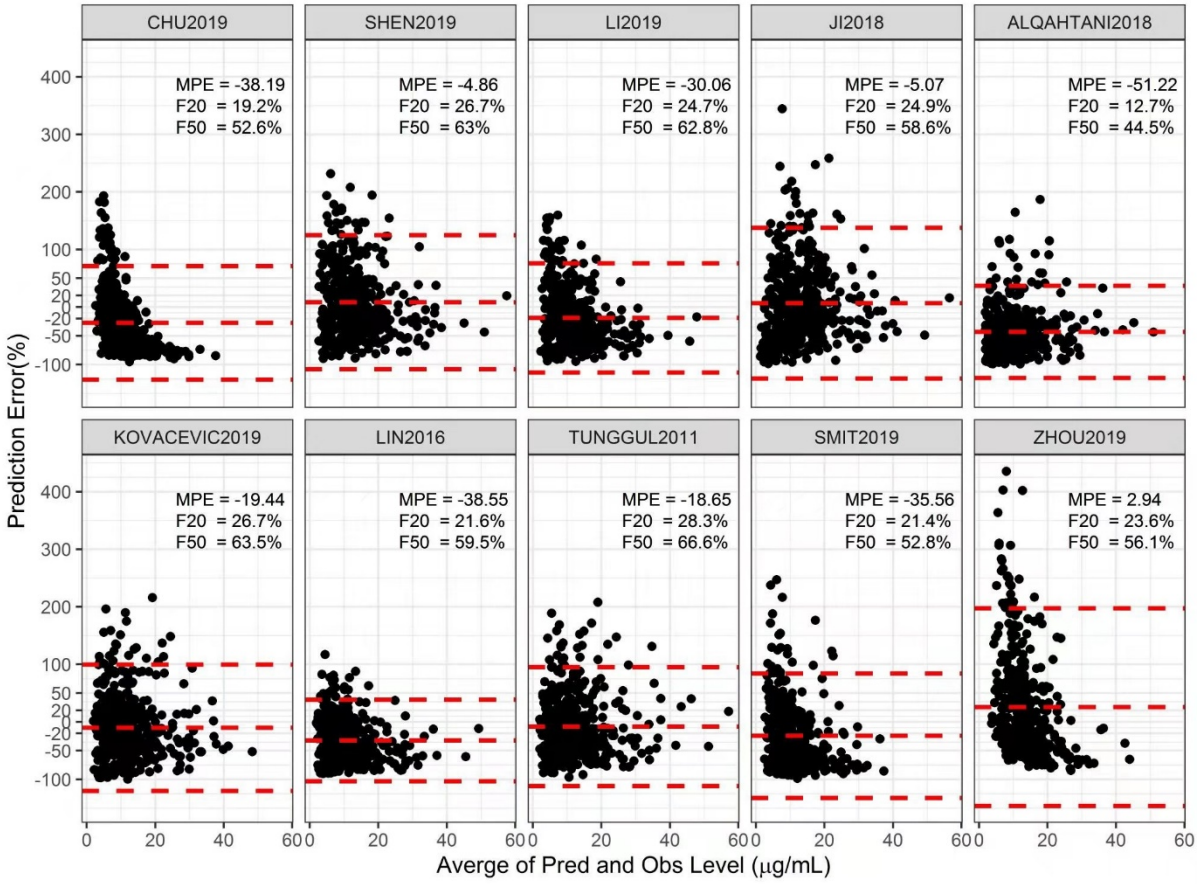
Objectives: Though extensive population pharmacokinetic (PPK) studies of vancomycin were performed to facilitate dose individualization, no clear consensus on optimal dosing has been achieved. The objective of this study was to perform an external evaluation of the published models, in order to assess their predictive performances in Chinese patients and to identify the potential influencing factors.
Methods: A literature search of Pubmed database was conducted to identify suitable models of vancomycin. The included models were evaluated by an independent dataset collected from 10 large cohorts of Chinese infected patients. Predictive performance was evaluated by visual comparison of observations and predictions, by calculation of imprecision and bias using prediction error (PE) and root mean squared error (RMSE), and factors influencing model predictability were explored.
Results: Ten published models were evaluated by 449 vancomycin serum concentration samples from 397 Chinese infected patients. In prediction-based diagnostics, half of the models had a median PE (MPE) within ±30%, among which the models by Ji et al, Shen et al and Tunggul et al showed relatively good accuracy and precision, with low RMSE (6.60%, 8.20% and 8.50%, respectively). The various factors influencing model extrapolation included the infection types, age, serum creatinine values and estimated glomerular filtration rate (eGFR) levels of the patients and vancomycin manufacturers.
Conclusion: Half of the vancomycin PPK models revealed acceptable accuracy and precision. Patient's infection sites, age, renal function, and drug manufacturers may affect the extrapolation effect of the models. In clinical practice, the models which study population closet to patient population should be selected, and sufficient external verification should be performed.


CHU2019
MPE = -38.19
F20 = 19.2%
F50 = 52.6%
SHEN2019
MPE = -4.86
F20 = 26.7%
F50 = 63%
LI2019
MPE = -30.06
F20 = 24.7%
F50 = 62.8%
JI2018
MPE = -5.07
F20 = 24.9%
F50 = 58.6%
ALQAHTANI2018
MPE = -51.22
F20 = 12.7%
F50 = 44.5%
KOVACEVIC2019
MPE = -19.44
F20 = 26.7%
F50 = 63.5%
LIN2016
MPE = -38.55
F20 = 21.6%
F50 = 59.5%
TUNGGUL2011
MPE = -18.65
F20 = 28.3%
F50 = 66.6%
SMIT2019
MPE = -35.56
F20 = 21.4%
F50 = 52.8%
ZHOU2019
MPE = 2.94
F20 = 23.6%
F50 = 56.1%
Prediction Error(%)
400
300
200
100
50
20
0
-20
-50
-100
0
20
40
60
Averge of Pred and Obs Level (μg/mL)

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Filter Lifespan in Continuous Renal Replacement Therapy

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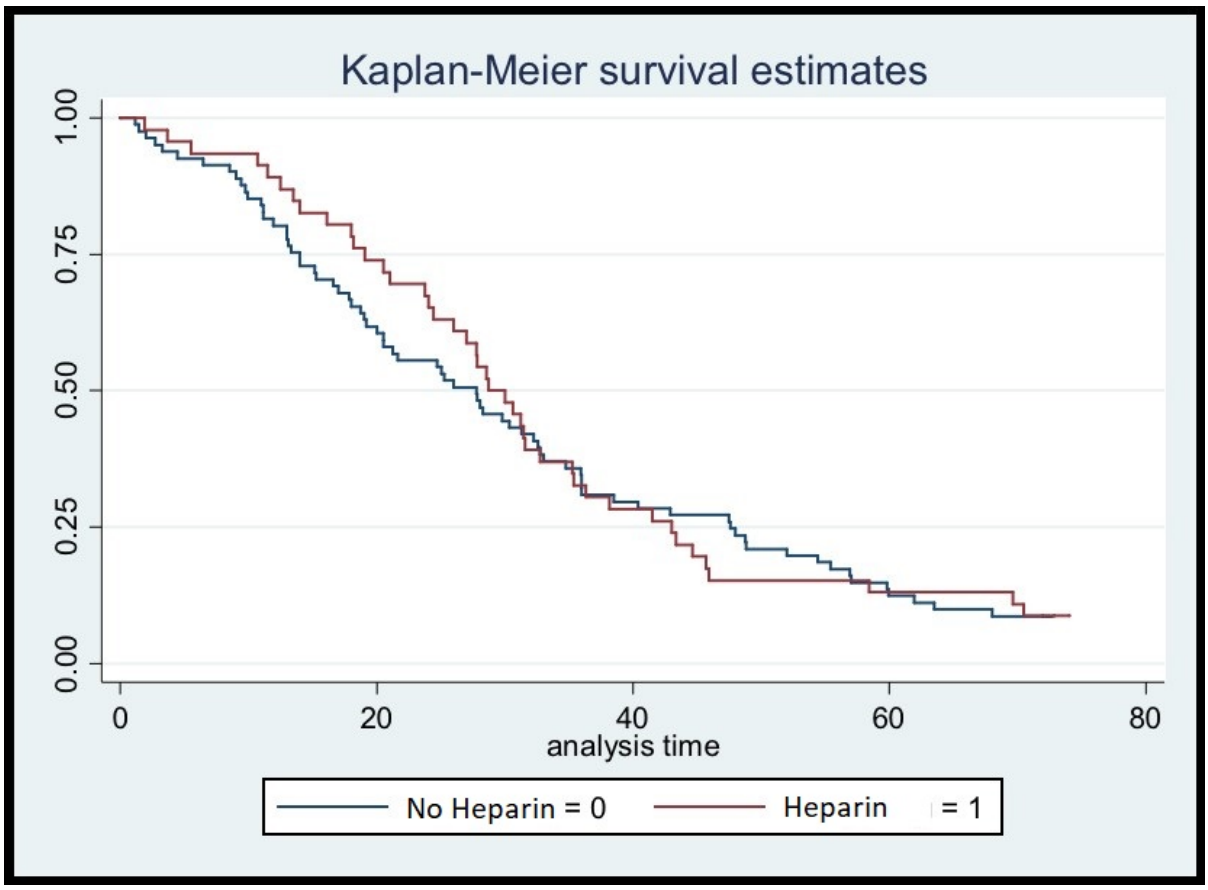
Objectives: To determine filter lifespan during the first CRRT session
Methods: Retrospective observational study. Patients aging over 18 years old admitted to intensive care unit from July 2019 to February 2020 at University Medical Center at Ho Chi Minh city, Viet Nam. Patients with chronic kidney disease with routine IHD or PD; performed CRRT or IHD before ICU admission; plasma exchange; discontinued first CRRT due to cardiac arrest, operation, imagine diagnostic (CT, MRI) or family request were excluded.
Results: This study included 127 cases with median aged 71 (61 – 82), 48.8% male. Mortality rate was 69.3%. Renal indications for CRRT were 80.3% and non-renal indications were 19.7%. All CRRT modality was CVVHDF. The most frequently used filters were M100 (96.9%). Four cases were performed CRRT with Oxiris (3.1%). Heparin was the only anticoagulation used. Rate of CRRT with anticoagulation was 36.2%. Median filter lifespan was 28 (15.2 – 44.7) hours. Three patterns of filter clotting were early (<10h), intermediate (10 – 24h) and late (>24h). Rate of filters in each group were 11.3%; 28.2% và 60.5%, respectively. Filter lifespan in anticoagulation group was nonsignificantly longer than group without anticoagulation (30.3 (19.5 – 43.2) hours vs. 27.8 (133 – 48) hours; p=0,33).
Conclusions: Filter lifespan during the first CRRT session was longer than 24 hours. Most of CRRT indications were renal causes. Mortality rate in CRRT patients was nearly 70%

Clotting pattern	All (N = 127)	M100 (n = 123)
Early (<10h)	4.4 (2 – 9)	4.9 (2.5 - 9.1)
Intermediate (10 – 24h)	16.4 (13.0 – 19.2)	16.6 (13 - 19.2)
Late (> 24h)	38.3 (30.4 – 58.1)	38.3 (30.5 – 58.8)



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The Effect of Transmembrane Pressure (TMP) on Solute Clearances in CVVH

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Introduction: A CRRT dose study established a clear relationship between CRRT dose and survival in the post-dilution mode (Ronco, Lancet 2000). The benefits provided by CVVH for both pre-dilution and post-dilution may be related to high MM clearances. However, solute clearances were not measured in the study, A careful assessment of the treatment factors, such as transmembrane pressure, influencing MM clearance in CVVH has not been performed. This study was to access the effect of TMP on the clearance of both SM (urea, creatinine) and MM (vancomycin, inulin) under different operational conditions. Materials and Methods: The Prismaflex

(Baxter) was used to create three different dilution modes, pre-blood pump (PBP), PRE and POST. Simulated treatment (N=3) involved 6 L of bovine blood (35% Hct, 36oC) processed at zero net ultrafiltration for a duration of 240 min. A 1.4 m2 filter (HF 1400) was used. The three experimental conditions: 1) blood flow rate QB: 190 mL/min; replacement flow rate QR: 2 L/hr, 2) QB: 290 mL/min; QR: 3 L/hr, 3) QB: 380 mL/min; QR: 4 L/hr. Conditions were chosen to maintain filtration > 25% in POST. Solute clearance at various time points were based on mass balance. Results and Discussion: The TMPs in different dilution modes are different. The POST had higher TMP than other two dilutions. PRE and PBP has no significant difference in TMP. There were linear relationships between TMP and solute clearance. The higher the TMP is, the larger the clearance is in all three dilutions. 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 high TMP in POST to low TMP in PRE and in PBP, although there were no significant differences between these two low TMP (PRE and PBP) for any solutes. In the PRE and PBP, the clearances of MM (inulin, vancomycin) are almost the same as in POST under different conditions. But in the PRE and PBP, the TMP values are much lower than in the POST with the same clearances. Increasing TMP in PRE and PBP to the same level of POST, one can expect a higher solute clearance. Conclusions: 1) higher clearance values for MM are obtained in PRE/PBP than in POST at certain TMPs. 2) The data obtained from PRE and POST are predictable for SM but are not consistent for MM. 3) SC of MM decreased substantially at higher TMPs & with time, likely due to secondary membrane effects.

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Changes in Cardiac Index in Critically Ill Pediatric Patients During Connection onto Continuous Renal Replacement Therapy.

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Background: Continuous renal replacement therapy (CRRT) is the preferred acute kidney injury (AKI) support modality in critically ill children. We and others have

shown hypotension and tachycardia occurs in 25-50% CRRT filter starts/changes as detected from bedside vital sign monitors. We aimed to investigate actual changes in cardiac index and other hemodynamic parameters using advanced hemodynamic monitoring.

Methods: Prospective study of pediatric CRRT patients between 11/2019 and 9/2020. Patients receiving combination or tandem therapies such as extracorporeal membrane oxygenation were excluded. Routine hemodynamic data were collected continuously 60 minutes before and after connection onto CRRT using archived high resolution physiology data (Sickbay, MIC Healthcare, Houston, TX), and advanced hemodynamic parameters were measured using electrical cardiometry (ICON, Osypka Medical, Berlin Germany). Hypotension was defined as a >20% decrease in mean arterial pressure (MAP) from baseline (baseline = mean MAP 60 minutes prior to connection). Primary outcome was decreased cardiac index after filter connection.

Results: 5 patients with a total of 7 connections were analyzed. The median age at ICU admission 70 months (IQR 8.5-139.5), median BSA 0.41m2 (IQR 0.71-1.44); 56% were female. Median PELOD 2 score was 7 (IQR 5.75-7). Primary reason for CRRT initiation was AKI with fluid overload 5/6 (83%) and the median starting CRRT prescription was 2000mL/hr/1.73m2 (IQR 2000-3500). Mean heart rate before and after connection was 125 beats per minute (bpm) (+/-18) and 122 bpm (+/-21) respectively (p=0.36). Mean MAP before and after connection was 81 mmHg (+/-18) and 76 mmHg (+/-16) respectively (p=0.15). Mean CI before and after was 4.93 L/min/m2 (+/-1.38) and 4.63ml/min/m2 (+/-1.21) respectively (p=0.28). Fifty seven percent (4/7) of connections had a drop in cardiac index (CI), with a mean decrease of 12.8% (+/-5.4%) after connection. Only 50% of decreased CI had concurrent overt hypotension.

Conclusions: CRRT filter connection represents a vulnerable period for hemodynamic changes in pediatric patients. Greater than 50% of connections had a drop in CI but only 50% of those had overt hypotension detectable through the bedside monitors. Future studies are needed to further investigate the risk factors associated with such adverse hemodynamic events, including the impact of CRRT prescription on cardiovascular and patient outcomes.

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Implementation Of Continuous Renal Replacement Therapy (CRRT) with COVID-19, Prismaflex to Prismax, and Citrate Anticoagulation

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Continuation of CRRT (Continuous Renal Replacement Therapy) minimizes patient hemodynamic instability and provides fluid balance. Studies have concluded that limiting disruptions and time off the machines produces the best outcomes for patients on CRRT and decreases the mortality rate.

Fresenius had informed our facility in April of 2018 that they would not be providing support for the Fresenius K machine effective December 2019. The K machine was the machine that was being utilized for 24-hour renal replacement therapy for the adult critical ill patients by the dialysis team. The Prismaflex was selected which was already being used by our Pediatric Nephrology team.

A mandatory completion of two online CRRT modules and attending training sessions provided by Baxter needed to be completed by the staff nurses. Documentation was on both paper and EPIC (The Electrical, Process, Instrumentation and Control Systems) for the CRRT patient assessment records. Data was gathered as part of a performance quality project and included the length of days the patients were on CRRT before changing the circuit and the reasons why the circuit was changed. An extension line was utilized for COVID-19 patients. The extension is 10 ft long which allowed the Primaflex to be out of the patient's room. The PrisMax machine was introduced in phase two of our CRRT hybrid model initiative and training was completed to both the ICU and dialysis team. The PrisMax and Prismaflex utilized the same filter circuits and were similar in set-up. The two items that differed between the two machines was that the PrisMax has a warmer piece that needed to be attached and an Auto-Effluent drain which eliminated the need to change effluent bags during CRRT, minimizing treatment disruption.

This study demonstrates that continuous CRRT without changing the circuit can lead to good patient outcomes such as transitioning to IHD and assisting with the overall

care of the patients. Mortality rate on patient on CRRT at LLUMC was 26% in 2019 and the average life of the CRRT circuits was approximately 24 hours. The utilization of citrate anticoagulation will be utilized to assist with the life span of the CRRT circuits. Citrate Anticoagulation: 140-180 mL/hr (Blood flow rate 100 mL/min) = Maintain Post-Filter Ionized Calcium at 0.25 – 0.3 mmol/L
Calcium Chloride Solution: 8 g Ca Cl in 1000 mL 0.9% Sodium Chloride 40 mL/hr = Maintain Peripheral Ionized Calcium 1.10-1.3 mmol/L.