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Blood Purification

1

Predictors of AKI and Mortality in Patients with Sepsis

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Background: Acute Kidney injury (AKI) is a common complication of sepsis in critically ill patients. Elevated levels of Endogenous Ouabain (EO), an adrenal stress hormone with hemodynamic effect, contributes to the development and maintenance of AKI in critically ill patients.

The aim of this study was to assess the role of EO and other markers to predict AKI and mortality in patients with sepsis and septic shock.

Methods: 177 patients diagnosed with sepsis or septic shock admitted in non-intensive care units were enrolled in 2010–2013 and 2019–2020. We assessed the role of different clinical and biochemical markers to predict AKI and mortality in patients with sepsis. In a subgroup of patients EO was measured at the hospital admission and for the next 48h.

Results: The incidence of AKI was 70,1%. Respiratory distress ($p=0,005$) and SOFA score at the onset of sepsis ($p=0,007$), resulted valid clinical predictors of AKI.

Lactate levels correlate well with SOFA (p -value $<0,0001$) and mortality particularly when the initial values are >2 mg/dL (p -value $0,003$). AKI seems not to predict mortality ($p=0,13$).

The initial EO value seems to predict mortality (p -value $0,02$) but not the development of AKI, however patients in AKI-stage 3 show persistently higher levels of EO.

Conclusions: Hypotension, SOFA score and respiratory distress at the onset of sepsis, are the main predictors of AKI while, serum lactate and SOFA score are the major predictors of mortality. EO may have a role in persistence of renal damage in conditions of severe hemodynamic alterations such as presence of septic shock. Its serum level is able to identify patients with more severe presentation and increased risk of early mortality and therefore, it may improve our ability to predict mortality in patients with sepsis.

2

Acute Kidney Injury in Patients Undergoing Hip Fracture Surgery

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Background: hip fracture is common in elderly patients and is associated with high morbidity and mortality. development of Acute Kidney Injury (AKI) following hip fracture may have additional impact on short- and long-term outcomes. We evaluated the incidence and the risk factors for AKI and its impact on clinical outcomes in patients undergoing hip fracture surgery.

Methods: we retrospectively examined the records of patients that underwent hip fracture surgery between 2013 and 2017 and had their serum creatinine measured upon admission and at least one follow-up value. AKI was defined according to KDIGO guidelines. we evaluated the incidence of AKI, the risk factors associated with its occurrence and its impact on clinical outcomes.

Results: 514 patients were included. Mean age 72.6 years. 325 (62%) males, 151 (29.8%) had baseline eGFR <60 ml/min/1.73m².

87(17%) patients developed AKI. The median rise in serum creatinine was 0.6mg/dl. (range 0.3–3.72 mg/dl) In univariate analysis: age (80.4 and 71.2 years in patients with and without AKI), prior CKD (median baseline eGFR 58.5 and 79 ml/min/1.73m² in patients with and without AKI), Diabetes Mellitus, Hypertension, and chronic heart condition were identified as risk factors for AKI.

Patients with AKI had increased risk of early (30 days) mortality {HR 3.96 CI [1.62–9.7] $p=0.003$ }; mortality at 12 months {HR 2.72 CI [1.5–4.9] $p=0.002$ }. AKI was an independent predictor of surgery delay for more than 48 hours after admission {HR 2.928, CI[1.602, 5.350] $p<0.0001$ } and was associated with longer hospitalization : mean LOS 10.9 days compared to 8 days in patients with and without AKI, $p<0.0001$.

Conclusions: AKI is a common complication in patients with hip fracture and is associated with increased short- and long-term mortality, delayed surgery, and longer hospitalization. Interventions aimed at identifying and monitoring patients at risk may contribute to improve the outcomes.

A Clinical Case of Fatal Goodpasture Syndrome in Young Uzbek Man

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A 26-year-old man of Uzbek ethnicity turned to the admission department of our clinic. He complained of a cough with scanty bloody sputum, swelling of the face, decreased urine, turbid urine, decreased appetite, weakness and general fatigue. In the anamnesis, he considers himself ill during the last 10 days, when the above complaints gradually began to appear. He went to a local hospital, passed tests and received outpatient treatment, which turned out to be ineffective. On examination in the office of the nephrologist revealed soft swelling on the face, arms and legs. When measuring blood pressure, hypertension is determined to be 170/100 mmHg. During auscultation of the lungs, fine-bubbly wet rales were heard over the entire surface of the lungs. The patient was hospitalized in the Department of Nephrology and was examined.

In blood tests, he revealed anemia (hemoglobin 75g / l, erythrocytes 2.7), leukocytosis, increased erythrocyte sedimentation rate. In a biochemical blood test, surprising to the patient, high levels of urea (20.1 mmol / L), creatinine (288.7 μmol / L) and residual nitrogen were found. The estimated GFR according to the CKD-Epi formula was younger than 25 ml/min. The total protein level was 65g / L. Indicators of blood electrolytes were within normal limits. Blood coagulation time remained at the upper limit of normal. Urinalysis determined high proteinuria (3.3 ppm), leukocyturia, erythrocyturia, cylindruria and bacteriuria. In the analysis of sputum revealed macrophages, white blood cells, red blood cells and bacteria. An ECG showed tachycardia, signs of left ventricular hypertrophy. Ultrasound examination determined hepatomegaly and an increase in kidney size and thickness of its parenchyma. A CT scan of the lungs revealed a diffuse bilateral interstitial lesion similar to Goodpaster syndrome. After the above analyzes, patients were diagnosed with *Goodpasture Syndrome, a rapidly progressing course. Respiratory failure 2 degrees.*

The patient was prescribed a strict diet and bed rest. The treatment was carried out with glucocorticoids: solomedrol (methylprednisolone) 1 gram daily for 3 days, after which the patient took prednisolone tablets at a dose of 1 mg per kg of body weight. Also, along with solomedrol, 1 gram cyclophosphamide was prescribed once. To improve blood rheology, heparin was used at a dosage of 5000 units four times (under the control of blood coagulation time) and dipyridamole in a daily dose of 325 mg. Of the antibiotics, ceftriaxone was prescribed at 2 grams per day and azithromycin at 500 mg per day. Furosemide, pentoxifylline, ascorbic acid, omeprazole, calcium D. were also prescribed.

During the treatment, the patient felt better and had an appetite. Swelling gradually decreased, the amount of urine increased, cough and sputum decreased. But azotemia increased, GFR decreased to 17 ml / min. The patient refused a possible replacement therapy - hemodialysis. In connection with a long stay in the hospital, the patient was discharged at will. Within 2 weeks, the patient was under control at home, the condition remained stable. But at 3 weeks after food poisoning and, as a result, diarrhea, the patient entered in a serious condition in the intensive care unit of our

clinic. In addition to dehydration, the patient showed impaired lung function, because of which he was connected to a ventilator. The state of the renal function also worsened progressively. Massive edema appeared and anuria developed. GFR was 3 ml / min.

Acute heart failure developed, followed by a decrease in heart function. Despite the resuscitation measure, it was not possible to save the patient's life. He died due to cardiac arrest.

COVID-19 as a Risk Factor for AKI Development: A Monocentric Experience

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Objective: evaluation of AKI prevalence and its associated-outcomes in all hospitalized patients during the COVID-19 pandemic at "Maggiore della Carità" University Hospital in Novara.

Methods: we performed an observational study based on data concerning patients admitted to our hospital between March and May 2020. We collected data from Board Hospital Discharge (BHD) and serum creatinine from the Lab data base. We performed AKI stratification in accordance to KDIGO criteria and we evaluated the outcome of different groups.

Results: we observed that 37,14% of all hospitals admissions showed the presence of AKI: indeed, we identified 351 AKI events COVID19-correlated; further sub-classified as follows: 173 AKI stage 1, 112 AKI stage 2 and 66 AKI stage 3.

Mean age for no-AKI group was 64.6 ys, 71.6 for AKI stage 1, 74.3 for AKI stage 2 and 67.9 for AKI stage 3.

Among the comorbidities evaluated only diabetes (p=0,048) and cognitive impairment (p=0,001) showed a significant difference for AKI development.

Mean eGFR at admission was 74.2 ml/min for no-AKI group, 64.3 ml/min for AKI stage 1, 57.8 ml/min for AKI stage 2 and 52.5 ml/min for AKI stage 3.

The mean length of stay for no-AKI group was 7.22 days, 13.67 for AKI stage 1, 15.83 for AKI stage 2 and 21.82 for AKI stage 3.

ICU admission rate was 5% for no-AKI group, 14% for AKI stage 1, 22% for AKI stage 2 and 44% for AKI stage 3.

In-hospital mortality was 27% for no-AKI group, 24% for AKI stage 1, 45% for AKI stage 2 and 42% for AKI stage 3 group.

Conclusion: AKI during the COVID19 pandemic impacts a large part of our admissions, with a higher prevalence in comparison to the epidemiological studies which we performed in 2018-2019: 37,14% against 17% and 18% respectively. In contradiction to the general characteristics of AKI patients, we did not observe a higher prevalence in elderly people and in patients with pluricomorbidities.

The presence of higher eGFR at admission could seem to be protective for AKI development.

The length of stay could seem to be dependent to AKI severity. ICU admission could seem to be linked to AKI development.

AKI stage 2 and stage 3 seemed to have a strong impact on mortality in comparison to the no-AKI group (OR 2.59 and 2.11 respectively against OR 0.27).

Logistic Regression Model for in-hospital death		
	OR	IC
Age	4,93	3,69–6,57
eGFR at admissions	0,2	0,15–0,26
Crs at admissions	1,26	0,15–0,26
Absence of AKI (no AKI group)	0,73	0,55–0,97
Length of stay	0,69	0,57–0,83
AKI stage 1	0,94	0,63–1,4
AKI stage 2	2,59	1,67–4,01
AKI stage 3	2,11	1,23–3,6

5

Polymyxin B Hemoperfusion Therapy and Extracorporeal CO₂ Removal in a Patient with COVID-19: A Case Report

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Background: A novel coronavirus, SARS-CoV-2, emerged in December 2019 in Wuhan, China. The coronavirus disease, COVID-19, became a pandemic and a major challenge to healthcare systems worldwide. Patients who are infected with SARS-CoV-2 may present with a wide range of clinical manifestations from mild, to moderate or severe illness. Severe cases may include severe pneumonia, ARF, ARDS, AKI, endothelial damage, coagulopathy, sepsis and septic shock.

Case presentation: A 54-year-old man with a medical history of obesity and hypertension developed fever, cough and diarrhea presented at the emergency department with fever and severe respiratory failure. The patient was asthenic and dyspneic and was immediately intubated and transferred to the ICU. Critical care management was initiated, including mechanical ventilation and vasopressors. A swab test for SARS-Cov-2 infection resulted positive. Tocilizumab and antibiotics therapy were initiated.

Blood cultures resulted positive for multi-resistant Gram-negative infection (*Acinetobacter*). Endotoxic shock was suspected (endotoxin activity assay, EAA, 0.92 EU), and two treatments with Polymyxin B hemoperfusion (Toraymyxin[®], Toray Medical Co., Ltd., Tokyo, Japan) were performed in 48 h. After two sessions the patient's clinical condition improved, EAA, procalcitonin, CRP and IL-6 decreased. Hemodynamic parameters also improved with increase in MAP and noradrenaline was suspended.

However, a week later the patient's conditions deteriorated. The patient became hypercapnic and in order to facilitate ultraprojective ventilation, extracorporeal CO₂ removal therapy was initiated and continued for 6 days resulting in improved PaCO₂ and increase of pH. The patient was hospitalized in the ICU for 113 days and was then admitted to a rehabilitation facility.

Conclusion: We have presented a case of COVID-19 complicated with septic shock and ARDS who in critical moments was treated with Polymyxin B Hemoperfusion and ECCO2R.

6

Polymyxin B Hemoperfusion in Septic Patients with Acute Myeloblastic and Premyelocytic Leukemia

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Background: Infections are frequent complications in patients with malignant hematological disease and are associated with high morbidity and mortality. The use of Polymyxin B hemoperfusion (PMX-HP) as an additional therapy in hematological patients who develop sepsis or septic shock following chemo- or immunosuppressive therapy is not often described in literature.

Methods: The study included patients with hematological neoplasms (acute myeloblastic or promyelocytic leukemia) who were undergoing chemotherapy (pre- or post-transplant) and developed sepsis or septic shock requiring organ support. The patients received one session of Polymyxin B hemoperfusion generally followed by at least 72 hours of CRRT as renal support. The patients clinical condition, hemodynamic parameters and blood chemistry values were monitored until discharge from the ICU.

Results: Nine patients were included in this study. Of the 9 patients, 6 survived and were discharged from the ICU. In the 6 surviving patients a drastic reduction in PCT and CRP were observed after treatment with PMX-HP. No adverse events related to the PMX-HP treatment occurred.

Conclusion: Patients with hematological neoplasms complicated with septic shock have a very high mortality. In our experience, Polymyxin B hemoperfusion therapy and CRRT in addition to conventional therapy seems to be a valid strategy to improve outcome in this type of patients.

Urinary Neutrophil Gelatinase-Associated Lipocalin (NGAL) in Critically Ill Patients with COVID-19

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Background: Acute kidney injury (AKI) has been reportedly associated with poor outcomes among patients with novel coronavirus disease 2019 (COVID-19). The efficacy of AKI biomarker for the management of critically ill patients with COVID-19 is unclear.

Methods: This retrospective observational study investigated urinary neutrophil gelatinase-associated lipocalin (NGAL) levels in ICU patients with COVID-19-associated respiratory failure. The outcomes of AKI development, mechanical ventilation requirement, and length of ICU stay were evaluated.

Results: Seventeen consecutive adult ICU patients with COVID-19 were included in this study. All patients presented with acute hypoxemic respiratory failure and required oxygenation; nine patients required mechanical ventilation (one patient soon turned to supportive care), and three of them used venovenous extracorporeal membrane oxygenation (VV-ECMO). Patients who developed AKI during ICU stay (N = 10) manifested significantly higher urinary NGAL levels at ICU admission than those without AKI (N = 7) (median, 93.0 vs 26.6 ng/mL; $p = 0.019$). The maximum urinary NGAL level within 48 hours from ICU admission was significantly correlated with the length of mechanical ventilation ($R^2 = 0.78$, $p = 0.004$) and ICU stay ($R^2 = 0.42$, $p = 0.009$).

Conclusion: This first report on urinary NGAL level in ICU patients with COVID-19 suggested its efficacy in predicting AKI development and duration of ventilator dependency. Urinary NGAL might reflect both kidney and lung injuries, caused by severe acute respiratory syndrome coronavirus 2 invasion in epithelial cells of these organs. Further studies are warranted to investigate the pathophysiology underlying the observed urinary NGAL level in patients with COVID-19-associated respiratory failure and AKI.

Use of Hemoadsorption in Cardiac Surgery.

Case Presentation

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Background: The contact of blood with the foreign surface of the cardiopulmonary bypass (CPB) used during open-heart surgery activates the production of inflammatory mediators and if it

is exaggerated, it can lead to multiple organ dysfunction in the postoperative period. Cytokine adsorbers have the ability to adsorb mediators, hence modulate these inflammatory processes. We present a patient who underwent redo cardiac surgery, in whom we applied hemoadsorption intra- and postoperatively to reduce postoperative inflammation and complications.

Methods: A 64-year-old female was admitted for elective surgery for dysfunction of mitral and aortic prosthesis and aortic aneurysm, pulmonary hypertension. Because we expected a long CPB time and a pronounced systemic inflammatory response (SIRS), intraoperative hemoperfusion was performed with HA330 cytokine filter during the CPB. Postoperatively hemoadsorption had to be repeated because of SIRS.

Results: Aortic and mitral prosthesis replacement and ascending aortic recalibration were performed. The length of the CPB was 277 minutes. On the first postoperative day, the patient had no signs of SIRS, but because of a low cardiac output, she required high doses of inotropic and vasoactive agents. The lactate level was high. The next day a pronounced inflammatory syndrome (CPR 30.8 mg/dL, PCT 9.8 ng/L, temperature 38.7 °C) developed, with hypotension and increased lactate level. We started hemoadsorption with HA330 cartridge. The patient's hemodynamic condition improved, the lactate level and systemic inflammatory signs decreased. After 2 days of ICU, the signs of SIRS became pronounced again, blood pressure decreased, requiring increased doses of vasopressors. After two hemoadsorption sessions the patient's hemodynamic status improved, lactate normalized and she could be extubated. On the 9th postoperative day the patient was transferred from ICU, on the 16th day she was discharged from the hospital.

Conclusion: The use of cytokine adsorber significantly reduces the severity of systemic inflammation and improve hemodynamic condition.

Clinical Characteristics and in-Hospital Outcomes for 1519 Consecutive Patients with AKI

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Introduction: Acute kidney injury (AKI) occurs in about 15% of hospitalized patients. Patients who recover from AKI have a higher long-term risk of end-stage kidney disease and death. The aim of this large single center study was to report differences in laboratory findings and short-term hospital outcomes in relation to cause of AKI in consecutive patients in a nephrology department.

Methods: All patients diagnosed with AKI between 2009 and 2018 admitted to the nephrology department at Danderyd University Hospital, Stockholm, Sweden, were included. Relevant laboratory and physiological measures were registered. Patients on

dialysis treatment were excluded. Patients were followed until discharge or death, whichever came first.

Results: In 1519 AKI patients, the majority (n=687) was of prerenal, followed by combined (defined as chronic kidney disease combined with any type of AKI) (n=536), renal (n=166), and postrenal (n=130) etiology. Patients with renal AKI were younger, had longer duration of stay, and had higher bicarbonate levels on admission. In-hospital reduction of sCr of at least 30% was seen in 63.2% of patients. Most of these had prerenal followed by postrenal etiology. There was no statistically significant difference in mortality between the four etiologies of AKI.

Conclusion: This study provides data from a large, contemporary AKI patient cohort. We confirm that patient characteristics as well as short-term outcomes differ substantially in patients of variable AKI etiology. Greatest in-hospital reduction of sCr was observed in patients with prerenal and postrenal AKI, whereas patients with renal and combined AKI had poorer renal recovery. These findings have important implications for prognostic evaluation upon admission and further resource planning.

10

The Use of Polymyxin B Hemoperfusion for COVID-19 Patients with Endotoxic Shock

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Background: Gastrointestinal dysfunction may lead to increased mucosal permeability and leakage of endotoxin. Although coronaviruses are known mainly as respiratory pathogens, up to 60% of COVID-19 patients show gastrointestinal symptoms at admission or developed during hospitalization. Recent published data show how endotoxemia and bacterial DNA are frequently found in patients with COVID-19 pneumonia, indicating that loss of intestinal barrier function can contribute to the pathogenesis of COVID-19. In addition, patients who are hospitalized for extended periods in an ICU are more prone to superimposed infections. In this retrospective analysis we report our experience of Polymyxin B hemoperfusion (PMX-HP) as complementary therapy for unresponsive endotoxic shock management in 5 patients with COVID-19 hospitalized in our ICU ward between February and April 2020. To the best of our knowledge, there is no data published yet concerning PMX-HP use in COVID-19 patients.

Methods: in the present case series, we evaluated the impact of PMX-HP as adjunctive therapy in a population of patients affected by COVID-19 and confirmed endotoxic shock identified by measurement of endotoxin activity at enrollment. Hemodynamics and main clinically relevant outcome parameters were monitored. PMX-HP treatment consists of 2 hemoperfusion sessions, the second session performed 24 hours after the first one, at a blood flow rate of 100 ml/min. Unfractionated heparin was used as standard anticoagulant.

Results: PMX-HP treatment was associated with rapid hemodynamic stabilization with reduction of Vasopressors Inotropic Score (VIS) – (from a mean value of $29 \pm 15,17$ to $2,60 \pm 2,88$ at 120 hours, $p < 0,05$), reduction in blood lactate levels (from $2,84 \pm 1,43$ to $1,08 \text{ mmol/l} \pm 0,54$ at 120 hours – $p < 0,05$), rapid decrease in Endotoxin Activity (EA) levels (from a mean EA value of $0,70 \pm 0,10$ to $0,49 \pm 0,13$ at 48 hours – $p < 0,05$) in a population affected by SARS-CoV-2 and endotoxic shock. PMX-HP treatment resulted safe and well-tolerated with no device related adverse events during or after hemoperfusion sessions. All patients received 2 hemoperfusion sessions.

Conclusion: Endotoxic shock could be associated to SARS-CoV-2. PMX-HP can be considered for management of unresponsive endotoxic shock. In our cases, PMX-HP treatment was associated with rapid hemodynamic improvement associated with a rapid decrease in vasopressor use, blood lactates and EAA levels. PMX-HP treatment was safe with no device-related adverse events.

11

When AKI Becomes CKD with Need for Substitutive Treatment in Preterm Low Birth Weight Newborns: Experience with a Miniaturized Device

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A baby boy born at 33+3 weeks of gestational age, 2,340 kg, was referred to our Division at 48h for oligo-anuria (urinary output: 0.4 mL/kg/h). The pregnancy was complicated by severe oligohydramnios and ultrasound suspect of posterior urethral valves, confirmed after birth. At birth the newborn experienced respiratory distress with anterior pneumothorax requiring mechanical ventilation. Serum creatinine was 1.6 mg/dl, with normal acid-base and electrolytes balance.

Maximal diuretic stimulus and cutaneous ureterostomy allowed only partial diuresis increase. Nevertheless, the gradual worsening of fluid overload and retentive indices, the persistent need for mechanical ventilation and the unstable hemodynamic status indicated renal replacement therapy (RRT).

Automated peritoneal dialysis (APD) was excluded due to ureterostomy presence and mechanical ventilation need in a low weight newborn. Continuous Renal Replacement Therapy (CRRT) was therefore started, with dialysis device CARPEDIEM[®] (Cardio-Renal Pediatric Dialysis Emergency Machine) choosing a continuous veno-venous hemodialysis program (CVVHD) with heparin anticoagulation. CRRT was continuously performed for 403 h, then intermittently (10 h/day) for 16 more days. In 10 days fluid

overload was resolved allowing weaning from mechanical ventilation; serum creatinine and urea concentrations were managed safely and effectively during all treatment. No metabolic, cardiovascular or thrombotic complications developed during CRRT.

At 36 days of life the baby was switched to APD and was discharged from the hospital at two months of life in good general condition, adequate development for being now at term, under chronic RRT with APD.

In conclusion, a prolonged CRRT with CARPEDIEM® device allowed safe and effective progressive stabilization of hemodynamics, gradual control of fluid overload and prolonged term blood purification, enabling the child growth to a size when APD could be started. The child is now 9 months old, with normal psychosomatic development, still under APD. He will be waitlisted for kidney transplantation when of adequate body size.

12

Acute Kidney Injury in Critically Ill Trauma Patients

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Background: Acute Kidney Injury (AKI) is a common complication in trauma with 24% of incidence in intensive care unit and it is independently associated with increased morbidity and mortality, but also prolonged length of stay. The high incidence of AKI in trauma patients should lead to early identification of those at risk of AKI to establish a resuscitation strategy that aims at preventing AKI.

Methods: Detailed data of trauma patients between May, 2017 and May, 2019 were retrieved from ICU medical records. In particular, patients' demographics, hemodynamic parameters, biochemical parameter and fluid balance, urinary output, sCr values at baseline, 24 hrs, 48 hrs, and 72 hrs. Short and long terms outcomes had been analysed.

Results: Based on KDIGO criteria, 45 patients developed AKI (29.4%). 16 patients (10.5%) developed stage 1 AKI, 29 patients (19.9%) stage 2–3 AKI. Patients with elevated urinary biomarkers alone undergoing therapeutics interventions had 8.5% stage 2–3 AKI compared to 33% of patients with creatinine elevation only, and 50% of patients with both increased creatinine and AKI risk score. A number of 19 patients (23%) with urinary markers driven interventions progressed to higher stages of AKI, while 7 (8.5%) improved AKI stage.

Conclusion: AKI is a frequent complication following trauma. Although the reduction of stage 2/3 AKI based on therapeutic interventions driven by elevated urinary biomarkers was observed in 8% of patients, the use of biomarkers represent an important tool for the early detection of patients at high risk of AKI behind the local ICU experience based on multidisciplinary team.

13

Predicting COVID-19 Acute Kidney Injury (AKI): The Role of Urinary Biomarkers. Bergamo ICU Experience

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Background: AKI is common in patients affected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurring approximately in 20–40% of cases⁽¹⁾ and it is independently correlated with mortality. Urinary biomarkers (tissue inhibitor of metalloproteinases-2 and insulin-like growth factor binding protein 7) measured by Nephrocheck® (NC) may play a role in early AKI detection⁽²⁾.

Aim: evaluate whether NC is able to predict the development of AKI in SARS-CoV-2 patients.

Methods: We prospectively enrolled seventeen mechanically ill ventilated SARS-CoV-2 patients, admitted to our ICU between March and April 2020. NC was performed at two time-points: at 4–6 hour and at 24 hours after ICU admission. NC > 0.3 and ≥ 2 defined a high or highest risk of development AKI in the following 12 hours, respectively⁽³⁾. Serum creatinine, urine output, central venous pressure (CVP) were collected daily for 7 days. AKI was defined using full Kidney Disease Improving Global Outcomes (KDIGO) criteria. The statistical analysis was made using the Mann-Whitney test.

Results: Twelve patients and two patients had NC value > 0,3 and ≥ 2 at ICU first sample, respectively. Four patients (23%) developed AKI and two patients needed CRRT. In four patients (23%) NC values normalized at 24 h. A NC value at admission ≥ 2 has a strong correlation with the development of AKI and a progression to AKI stage ≥ 2 (p = 0,02). Patients with NC > 0,3 at admission have central venous pressure (CVP) values higher than patients with NC < 0,3 (p < 0,05).

Conclusion: Although a small study population, our data suggest that a NC value ≥ 2 at ICU admission is associated to a high risk of AKI. High CVP levels are associated to higher levels of NC, suggesting a role of high CVP in predicting AKI risk.

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The Five-Year Prognosis in Patients with Contrast-induced Acute Kidney Injury and Stable Coronary Artery Disease

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Aims: The aim of the study was to assess the incidence and influence of contrast-induced acute kidney injury (CI-AKI) and different risk factors on 5-year prognosis in patients with stable coronary artery disease undergoing PCI.

Methods and Results: The prospective, cohort, observational study (ClinicalTrials.gov ID: NCT04014153) included 2 groups assessing 1-year and 5-year prognosis in patients with stable coronary artery disease (CAD) receiving optimal medical treatment and requiring PCI with iodinated contrast media. All the patients randomly received iodixanol (iso-osmolar contrast) or iopromide (low-osmolar contrast).

CI-AKI was defined as an increase of 25% or more, or an absolute increase of 0.5 mg/dl or more in serum creatinine from baseline value, assessed at 48 hours following PCI (according to the 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury).

The 5-year prognosis bundle included 561 patients aged 18-89. The prevalence of male patients developing CI-AKI was higher than female 72 (69%) vs. 32 (31%), but the difference was statistically insignificant ($p < 0.05$). 24 patients (23%) who met the criteria of CI-AKI suffered from diabetes mellitus and only 9 (37.5% of all the patients with diabetes) received metformin. Only 1 female patient died during the hospitalization due to myocardial infarction. 10 patients (42% of all the patients with diabetes and CI-AKI) had repeat revascularization (repeat PCI) mostly in the first 1-2 years after the date of inclusion compared to 43 (41%) of all the patients with CI-AKI. So the rate of repeat revascularizations was almost the same in patients with and without diabetes. 29 patients (28%) suffered from myocardial infarction. The overall rate of myocardial infarction during follow-up period of 5 years was 13% (73 cases), so two times lower than in CI-AKI group. 5 patients (4.8%) suffered a stroke after the episode of CI-AKI. 11 patients with CI-AKI (10.6%) had episodes of decompensation of chronic heart failure during the follow-up period.

Anemia was diagnosed in 7 patients with CI-AKI (6.7%) and did influence the 5-year prognosis statistically significantly ($p = 0.0013$). As well as chronic heart failure diagnosed in 8 patients on admission (7.7%) ($p = 0.0001$).

Conclusions: The incidence of CI-AKI was 104 cases (18.5%). Gender and diabetes did not statistically significantly influence the 5-year prognosis in our study. Anemia and heart failure on admission were associated with statistically significantly worse prognosis in our group of patients with CI-AKI. Larger groups are needed to define the importance of potential risk factors influencing the outcomes in patients who develop CI-AKI during planned PCI procedures in patients with stable coronary artery disease

The Application of Continuous Renal Replacement Therapy (CRRT) Beyond Acute Kidney Injury (AKI) Among Critically Ill Children with Malignancy

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Background: The role of CRRT has been expanding beyond acute renal support in recent years. Children with malignancy are at risk of developing various conditions requiring CRRT in addition to acute kidney injury.

Methods: We reviewed the medical records of oncology patients requiring CRRT for non-AKI indication in the Hong Kong Children's Hospital between 3/2019 to 9/2020.

Results: Three patients were identified (Table 1). Except mild electrolytes disturbances, no major CRRT-related complication was encountered.

Patient 1: A 17-year-old girl with relapse of B-cell acute lymphoblastic leukaemia (ALL) developed refractory lactic acidosis with peak lactate level 18mmol/L and lowest pH and bicarbonate level 7.13 and 6.0mmol/L. High-volume haemodiafiltration was started as a bridging therapy before chemotherapy started to work. The measured mean lactate clearance was 65ml/kg/hour.

Patient 2: A 15-year-old male with T-cell ALL developed peritonitis and pneumoperitonium complicated with Klebsiella pneumoniae septicaemia. He remained critically ill despite multiple anti-microbials, high dose inotropes and a dose of intravenous immunoglobulin. Hence haemoperfusion using the Oxiris® filter was performed for endotoxin removal. The inotropes were then weaned off, and his condition was gradually stabilized. Resection of the remaining necrotic small bowel was performed 3 days later.

Patient 3: An 8-year-old boy with bone marrow transplantation received for B-cell ALL gradually developed conjugated hyperbilirubinaemia with peak total and direct serum bilirubin level up to 305 and 263µmol/L due to veno-occlusive disease (VOD) and graft-versus-host disease (GVHD). He received a session of single-pass albumin dialysis using 4% albumin as dialysate as a temporary measure to reduce his bilirubin level, bridging him to receive a liver biopsy that confirmed the diagnosis of hepatic acute VOD and GVHD.

Conclusion: The role of CRRT in managing various complications of children with oncological diagnosis has expanded beyond traditional renal indications, and selected patients can be benefited from these techniques. However, the optimal dose, timing of initiation and monitoring target are largely unknown.

Acute Kidney injury Complicating Lactic Acidosis in a Patient Receiving Metformin, Lenalidomide and Telmisartan

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Background: Metformin is the first choice hypoglycemic drug in Type II Diabetes (T2D). However, metformin must be carefully managed inpatients with reduced renal function due to the risk of lactic acidosis. We hereby present a case report of lactic acidosis related to an improper use of metformin.

Presentation: A 77-year-old woman with T2D, Hypertension, Chronic Kidney Disease (CKD) stage III and Multiple Myeloma, was hospitalized due to the sudden appearance of vomiting, edema and asthenia. She was on home therapy with telmisartan+hydrochlorothiazide, lenalidomide and metformin 1.5 g/day. On admission, laboratory exams showed plasma concentration of: creatinine 6,37 mg/dL (eGFR 6 ml/min/1.73m²), BUN 173 mg/dL, phosphate 7.9 mg/d, arterial pH of 7.14, bicarbonates 6 mmol/L, lactate levels of 15.4 mmol/L with an anion gap of 30 mmol/L. After right jugular catheter placement, a Sustained Low Efficiency Dialysis (SLED) session was started with Blood Flow of 200 ml/min and Dialysate Flow of 300 ml/min. At the end of the session, pH improved up to 7.38, serum bicarbonates increased up to 19.7 mmol/L and lactates were reduced to 7.4 mmol/L. After a following session of CVVHDF, lactate plasma levels and the pH finally reverted to normal values. Ten days after, serum creatinine decreased to 1,5 mg/dl.

Discussion: Balancing metformin dosage is crucial in individuals with CKD. In fact, this patient was on exceedingly high doses of this drug, despite no overdose episodes have been previously recorded. Further worsening of renal function -probably induced by lenalidomide, dehydration and the concomitant therapy with losartan- may have significantly contributed to the progressive accumulation of the drug.

Conclusion: The reported mortality associated with metformin-induced lactic acidosis is high (~30%), particularly if AKI occurs. In this patient, despite the concomitant treatment with lenalidomide, we were able to achieve a favorable outcome by employing a combined SLED-CVVHDF approach.

Dialysis Strategies for AKI in Paroxysmal Nocturnal Hemoglobinuria

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disease that presents an estimated incidence of 1.3 cases per million per year. It is characterized by hemolysis, bone marrow dysfunction with peripheral blood cytopenia, hypercoagulability, thrombosis, renal impairment and arterial and pulmonary hypertension.

PNH-related AKI is due to the interaction and aggregation of hemolysis products and Tamm-Horsfall protein, leading to production of tubular casts. These, in turn, cause intratubular obstruction and damage, inducing an inflammatory response, resulting in interstitial nephritis and fibrosis.

In order to remove high molecular weight solutes and protein-bound uremic toxins, high- and medium-cutoff membranes, convective therapy and protein adsorptive membranes can be useful tools in PNH-related AKI. Convective technique is directly linked to plasma ultrafiltration and dependent on the specific solute sieving coefficient and on membrane permeability. The backfiltration mechanism represents a crucial mechanism in the removal of medium-high solutes during ultrafiltration. During HD treatment with a high-flux dialyzer, there is a large drop in blood compartment axial pressure that leads to a blood compartment pressure lower than the dialysate compartment pressure. The use of membranes with major permeability, larger pore size and decreased hollow-fiber inner diameter amplifies the internal filtration during the HD session, improving the clearance of large-solute compounds. In the proximal section of the dialyzer, this mechanism promotes convection effect; at the same time, backfiltration will compensate in the distal part. An ideal dialytic prescription to reach these results should guarantee at least a 300 mL/min blood flow with a dialysate flow of 500 mL/min or higher.

Methods: A promising alternative for current dialysis strategies in the course of AKI in PNH is represented by Coupled Plasma Filtration Adsorption (CPFA), a detoxification technique combining a plasma adsorption circuit with CVVH. The circuit is made of a plasma filter, a resin-adsorbent cartridge and a hemofilter. The goal of this treatment is to restore normal immune function by non-selectively adsorbing either pro- and anti-inflammatory mediators, and the greatest result is achieved with substances with high or medium molecular weights.

CPFA includes 5 steps:

- 1 Blood predilution with a replacement fluid to prevent clotting in the circuit.
- 2 A fraction of plasma is separated from blood with a plasma filter and then runs through the adsorbing cartridge.
- 3 The cartridge non-selectively removes almost all of the pro and anti-inflammatory mediators and endotoxins.

- 4 Plasma rejoins the rest of blood passing through a standard hemofilter.
- 5 Postdilution replacement fluid is eventually added to the purified blood and re-infused into the patient.

Results: CPFA can play a major role for PNH patients by the adsorption of hemolysis products, removal of inflammatory mediators and treatment of AKI, with the concomitant action of CVVH.

Conclusion: PNH is characterized by a plethora of insidious symptoms and damage mechanisms such as hemolysis, peripheral cytopenia, bone marrow dysfunction, thrombosis, arterial and pulmonary hypertension. Kidney involvement is a common feature of PNH patients but despite the increased knowledge of this syndrome, the most appropriate strategy and choice of therapies are still up for debate. The nephrologist has the task of choosing the most suitable treatment to modulate complement activation and plays a leading role in managing the dangerous possibility of AKI. Valid options are represented by immunoadsorption, hemodialysis filters that use convective techniques, backfiltration and CPFA.

18

The Role of Short-Term, High-Dose Atorvastatin for Prevention of Contrast-induced Acute Kidney Injury (CI-AKI) in Patients with Cardiovascular Diseases Undergoing Computed Tomography with Intravenous Contrast Administration

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Background: Computed tomography with intravenous contrast media is widely used in hospitals. The incidence of CI-AKI due to intravenous contrast media administration in high-risk patients remains not studied as well as CI-AKI after intraarterial contrast media administration is. According to other researchers, the use of statins in the prevention of AKI after intra-arterial administration of a contrast agent is currently considered an efficient preventive measure. The aim of our study is to assess the incidence of contrast-induced acute kidney injury in patients with cardiovascular diseases during CT scan with intravenous contrast media and analyze the efficacy and safety of various statin dosing regimens for prevention of CI-AKI.

Methods: A randomized controlled open prospective study is planned. Statin naive patients with cardiovascular diseases will be divided into 3 groups. Patients in the first group will receive atorvastatin 80mg 24 hours and 40mg 2 hours before CT scans and 40 mg after. The second group – 40 mg 2 hours before CT scans and 40 mg after. A third group is a control group. Exclusion criteria were current or previous statin treatment, contraindications to statins, severe renal failure, acute coronary syndrome, administration of nephrotoxic drugs. The primary endpoint will be the development of CI-AKI, defined as an increase in serum Cr concentration 0.5 mg/dl (44.2 mmol/l) or 25% above baseline at 72 h after exposure to the contrast media.

Results: we assume that high-risk patients receiving statins before CT scans with intravenous contrast administration will have a lower incidence of CI-AKI compared to the control group.

Conclusion: As a result of the study, we expect to conclude the benefits of statins in CI-AKI prevention and the optimal dosage regimen. This information will help us to reduce the burden of CI-AKI after CT scanning in statin naive patients with cardiovascular diseases in everyday clinical practice.

19

Rocuronium intoxication in intensive Care Patients with Severe Renal Impairment: The Synergistic Effect of Sugammadex during Dialysis Treatment with High Flux Membranes

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Background: Sugammadex antagonizes the neuromuscular block induced by Rocuronium binding it into a hydrophilic complex eliminated only by the kidney. This case report shows the efficacy of Sugammadex administration during hemodialysis with high-flow filters.

Case presentation: 71 year old male, obese, affected by Type 2 Diabetes Mellitus, Ischemic Heart Disease, Chronic Renal Failure (serum creatinine: 2.6 mg/dl), was admitted to Intensive Care for Respiratory Failure caused by *Legionella Pneumoniae* infection; he was treated with ExtraCorporeal Membrane Oxygenation (ECMO) and maintained in a regimen of treatment with Rocuronium (in continuous infusion) for 8 days. At the hospital admission: preserved diuresis, hyperbilirubinemia and hypertransaminasemia. 24 hours after the suspension of Rocuronium, failure to resume spontaneous breathing without signs of lateralization. TOF (Train of Four) stimulation showed complete neuromuscular block (TOF 0) and Post Tetanus stimulation confirmed lack of neuromuscular activity. Suspecting Rocuronium intoxication, Sugammadex (2 mg/kg) was administered with an increasing dose. At doses up to 16 mg/kg, the TOF indicated a partial and temporary reversal of the neuromuscular block. During the following day, development of Acute Renal Failure with anuria. Sustained Low-Efficiency Dialysis (SLED) with high flux membranes (Bellco HF17G filter; ultrafiltration coefficient: 53 ml/h/mmHg) was started administering Sugammadex (16 mg/kg) every 15 minutes. After 260 minutes of treatment, TOF monitoring showed a lasting resumption of neuromuscular activity.

Discussion: the prevailing hepatic metabolism of Rocuronium favors its accumulation in conditions of Hepatic Insufficiency. Sugammadex induces the elimination of curare via the kidney rather than via the liver. In case of severe renal impairment, the

reduced excretion of the Sugammadex-Rocuronium complex justifies the ineffectiveness of Sugammadex and the failure to reverse the neuromuscular block.

Conclusion: the administration of Sugammadex during SLED with high-flux membranes, favors the clearance of Rocuronium, enhancing the effectiveness of the dialysis treatment.

20

Incidence of Acute Kidney injury in COVID-19 Patients Receiving Noninvasive Mechanical Ventilation Outside intensive Care Unit: a Multicenter Study

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Objective: Pneumonia is the main clinical manifestation of Coronavirus disease 2019 (COVID-19). However, concomitant multi-organ injury related to SARS-CoV-2 infection are reported. Acute kidney injury (AKI) occurs in 20% of patients with acute respiratory syndrome. We report the cumulative incidence and outcomes of AKI in patients receiving noninvasive continuous positive airway pressure (CPAP) ventilation outside intensive care unit.

Methods: In this retrospective multicenter cohort study, we enrolled COVID-19 patients treated with noninvasive CPAP ventilation in five hospitals of Eastern Piedmont region from March 1st to April 15th, 2020. The primary outcome was to evaluate cumulative incidence of AKI in this population and to report demographic and clinical data including hospital length of stay (LOS) and 60-day in hospital mortality. Increase of serum creatinine was used for AKI definition.

Results: We included 449 COVID-19 patients treated with CPAP. The median age was 69 [59-75] years, and 332 (74%) were male. A total of 225 patients (50%) developed AKI at any stage. AKI patients compared to those without AKI presented a higher incidence of chronic arterial hypertension and diabetes *i.e.*, 123 (54%) *vs.* 104 (46%) and 68 (30%) *vs.* 49 (22%), respectively. At hospital entrance, serum creatinine was higher in AKI compared to non-AKI group *i.e.*, 1.04 [0.82-1.4] *vs.* 0.93 [0.75-1.17] mg/dL. Hospital LOS was higher for patients with AKI 21 [11-34] *vs.* 13 [7-21] days. In addition, 60-day in hospital mortality was higher in the AKI group 40% *vs.* 27%. Among patients scheduled to receive invasive mechanical ventilation (iMV) in case of CPAP failure, AKI was more frequent in those who received iMV 60% *vs.* 40%.

Conclusion: AKI is a common complication among COVID-19 patients requiring CPAP respiratory support. Patients developing AKI have a prolonged hospital stay and a higher mortality rate.

21

A Case of Metformin induced Lactic Acidosis Resolved with the Use of CRRT

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Introduction: metformin induced Lactic acidosis is an uncommon but serious condition with an incidence of 2-9 cases / 100,000 patients a year and high mortality (30%). The use of metformin for over half a century makes the drug safe and effective as a first treatment in type 2 Diabetes mellitus (T2DM), also due to its pleiotropic effects.¹ Lactic acidosis has been reported as an adverse event. Subjects in whom lactic acidosis has been diagnosed often have co-morbidities or risk factors that contribute to the development of acidosis.

Case report: an 84-year-old male patient enters the emergency room for abdominal pain and cough. Altered renal function tests (Creatinine 3.2 mg/dl and Urea 132 mg/ dl) and severe metabolic acidosis (pH 6.892, BE - 27.3 mmol /L, pCO₂ 29.8 mmHg, HCO₃ 5.70 mmol/L) were found. His medical history was remarkable for DM2 being treated with metformin, dyslipidemia, hypertension and episodes of acute coronary syndrome, for which he had undergone 3 aortocoronary bypasses. Given the finding of hypotension (70/40 mmHg), anuria and hemodynamic instability, treatment with noradrenaline and continuous CRRT dialysis in the CVVHDF module was started. 54 hours after the start of this treatment there was an improvement in the clinical picture with an increase in bicarbonates and blood pressure and a resumption of diuresis.

Conclusion: in case of metformin-induced lactic acidosis, treatment with CRRT in the CVVHDF form in order to combine diffusive and convective action over a long duration to remove any highly compartmentalized substances or substances with a high volume of distribution, and to implement a slow and gradual correction of acidosis, avoiding rebound phenomena as much as possible, represents a useful approach for the management of this uncommon but severe condition.

22

AKI Due to Rhabdomyolysis in Narcotic Drug-User Patient

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Background: medications, illegal drugs and toxins are the most frequent non-physical causes of rhabdomyolysis (RM). Acute kidney injury (AKI) is a serious and, sometimes, fatal complication of rhabdomyolysis; it occurs in about 8-20% of RM incidents. [1]

Table 1. Blood test during the hospitalization.

	ER	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
blood urea mg/dL	152	152	138	139	88	88	59	152	142	122
sCr mg/dL	7.2	7	5.7	5.9	3.3	3.1	1.8	3.4	1.9	1.4
CPK UI/L	15000	14660	16292	9682	2317	860	478	137	63	54
LDH U/L	1249	1149	1454	1338	948		1135	872	660	531
CK-MB UI/L			280	226		44	42	17		14
Na/K mmEq/L	140/4	140/3.9	139/3.7	140/4.4	139/3.9	136/4.2	140/3.8	138/3.7		138/4.1
Ca/P mg/dL	7.8/6	7.8/5.5	7.5/4.8	9/5.3	8.4/2.8	8.9/2.8	9.8/1.7			9/2.2

Case report – 47 old male patient came to our ER, unconscious with hypotensive state. We were told the patient was a usual narcotic-drug user. Vitals at the arrival were: blood pressure 68/40mmHg, HR 81bpm, spO₂ 92%, afebrile. Patient was oligo-anuric, pupils were miotic. The patient underwent to infusion therapy with saline solution and a vial of Naloxon 1mL/0.4mg was administered. Blood test showed: pH 7.186, HCO₃ 13,0, BE -16,7, pCO₂ 30.6mmHg, pO₂ 100%.

ECG showed aspecific changes on AV conduction and cardiac repolarization. Chest X-Ray showed pulmonary thickening in the middle pulmonary area. The patient was moved to our Nephrology Department and he underwent to central vein catheterization to start CRRT with CVVHDF mode.

CRRT was performed for 3 days (treatment was just interrupted to do CT scan, due to abdominal pain referred by the patients), dopamine was used to maintain adequate blood pressure; diazepam was administered in continuous to prevent withdrawal. Clinical condition slowly got better until the recovery of renal function with adequate urinary output (day 4) and normalization of blood pressure values.

Conclusion: AKI is one of the most severe complications of rhabdomyolysis. The initiation of RRT in clinical practice should be managed by the status of renal impairment, with life-threatening complications not-responding to clinical measures. In this case, CRRT represented the best therapy to treat AKI due to RM achieving the recovery of renal function.

[1] Acute kidney injury due to rhabdomyolysis in narcotic drug users, George Kosmadakis 1, Otho Michail, Vasileios Filiopoulos, Panoraia Papadopoulou, Spiridon Michail. PMID: 21786249 DOI: 10.5301/IJAO.2011.8509.

23

2 Hours Urinary Output before Starting CRRT as an Early Marker of Survival in AKI Patients in ICU

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Background: The aim of our study was to evaluate the role of urinary output (UO), 2-hours (hrs) before starting of continuous renal replacement therapy (CRRT), as an early marker of survival on critically ill patients hospitalized in intensive care units (ICUs).

Methods: Our study was performed on a wide historical Korean cohort of ICU patients with CRRT-requiring acute kidney injury (AKI). Clinical, demographic and laboratory data were collected for each patient. From original cohort were removed all patients with missing data at baseline. Our exposure of interest was the 2hrs-UO (collected before starting CRRT), divided in quartiles and reported as categorical variable in regression models. The outcome of interest was 90-days mortality. Cox regression model, adjusted for potential confounders (Table 1), was used to derive hazard ratios (HRs) and 95% confidence interval (CI). Restricted cubic spline (multivariable adjusted) was performed to describe the relationship between UO (reported as continuous variable) and log-HR of death 90-days mortality.

Results: 675 patients were included in the study. Higher 2hrs-UO was significantly associate with increased 90-days mortality (p value for trend = 0.002; Table 1, Figure 1). Multivariable adjusted Cox regression model demonstrated a reduced risk of 90-days death in patients in the higher quartile of 2hr-UO (HR 0.64, CI 95% 0.49, 0.85, p=0.002, 4th quartile compared with the 1st quartile [reference group]; Table 1).

Conclusion: 2hr-UO before starting of CRRT is an important early marker of survival in AKI patients in ICUs.

ACUTE KIDNEY INJURY in Critically Ill Patients with COVID-19: Our Experience. Preliminary Results

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Background: Patients with severe forms of COVID-19 may develop multiple organ dysfunction syndrome, including Acute Kidney Injury (AKI). We report the cumulative incidence, risk factors, associations and outcomes of AKI and renal replacement therapy (RRT) in critically ill COVID-19 patients.

Methods: We performed a retrospective cohort study of adult patients with COVID-19 diagnosis admitted to the intensive care unit (ICU) between February 21st and April 26th, 2020. The primary outcome was to evaluate the AKI cumulative incidence in our population. Multivariable Logistic Regression Analysis was applied to identify risk factors for the development of AKI.

Results: 45 (53%) patients developed AKI any stage by seven days from the ICU admission and 42 (93.3%) received RRT. AKI categorised by KDIGO stage are showed in Table 1. AKI patients were slightly older than no AKI patients, but gender, comorbidities were equally distributed in the groups. At the ICU discharge, 22 (27%) were classified as AKD and 7 (17%) as AKI patients. All these patients needed still CRRT (dialysis dependence). Intra-hospital mortality was higher in AKI patients compared to no AKI patients (27 (60%) AKI patients vs 15 (37%) no AKI patients $p = 0.038$). In multivariate analysis lopinavir/ritonavir administration was the main risk factor associated with the AKI development (OR 7.59 95% CI 1.51-38.0, $p=0.014$).

Conclusions: AKI was common among critically ill COVID-19 patients occurred in lightly older patient. In our population, gender did not affect AKI occurrence. Most AKI patient needed RRT (42 (93%) and at ICU discharge 27% showed AKD and 17% RRT dependence.

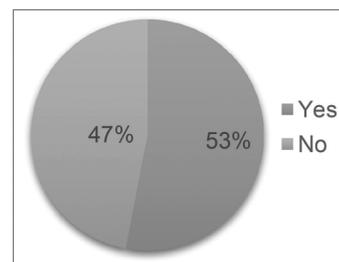


Fig. 1. AKI prevalence in COVID-19 positive patients.

Table 1. AKI according to KDIGO stage.

AKI stage	Freq (N)	Perc (%)
0	40	47
1	18	21
2	3	4
3	24	28
Tot	85	100

25

Hemoperfusion with JAFFRON HA330 as Life-Saving Treatment in COVID-19 Patients: 2 Case Reports

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Introduction: We report two cases of middle aged patients with ARDS related Covid-19 that needed ECMO support. Both received standard therapy (sedation, curarization, enteral nutrition and protective mechanical ventilation); antibiotics prophylaxis with piperacillin/tazobactam and azithromycin were prescribed and, if CD4+ count was lower than 500 cell/microliter, sulfamethoxazole/trimethoprim was added.

Table 1. Parameters before and after HP.

Variables	Patient 1		Patient 2	
	Pre-HP	Post-HP	Pre-HP	Post-HP
Lymphocytes cells/ μ L	476	1740	616	937
NK cells/ μ L	29	170	69	100
CD4+ cells/ μ L	212	858	293	500
CD8+ cells/ μ L	80	300	28	125
RCP (mg/dL)	14.37	3.24	36.54	14.84
PCT (ng/mL)	3.85	2.38	7.12	1.65
Lactate (mmol/L)	4.8	2.2	2.1	1.8
IL-2 (pg/mL)	67.41	14.1	67.41	0.1
IL6 (pg/mL)	425.15	259.47	325.75	259.47
IL-10 (pg/mL)	221.11	171.4	161.11	186.66

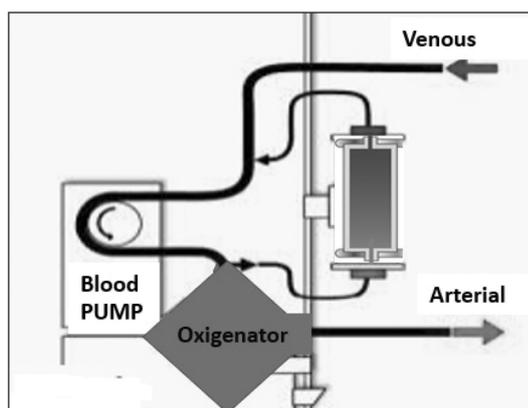


Fig. 1. Connection of HP cartridge to ECMO circuit (no CRRT device) in patient 1.

Case 1: The first case is an obese, 54 years-old man, without any comorbidities. After pronation and iNO, he required VV-ECMO (on day 11). We administered 2 doses of convalescent plasma (day 4 and 23) also. However, severe septic shock occurred and we shifted to VAV-ECMO (day 28). In this context, we performed 2 sessions of HP with Jaffron HA330, directly connected to ECMO circuit (Figure 1). Immediately after the sessions hemodynamic parameters, lactate levels and procalcitonin improved; all cytokines decreased. After 6 days, we noted an improvement of innate immune response (Tab I, patient 1). Unfortunately, a second septic shock due to coinfection of *Candida Parapsilosis* and *Acinetobacter Baumannii* resulted in MOF and death, 20 days later.

Case 2: The second case describes the case of an obese middle age man (51 years-old) with no comorbidities. In addition to stan-

ard therapy, remdesivir had been administered for 14 days. VV-ECMO was started on day 4. Two sessions of HP (Jaffron HA330) were performed (day 4 and day 5), combining ECMO and CRRT device. After HP, procalcitonin, RCP, hemodynamic parameters and lactate improved. We measured an improvement of the CD4+, CD8+ and NK counts, again (Tab I, patient 2). In one session, we evaluated the extraction ratio of the cartridge, which decreased over time except for IL-10 (data confirmed by plasma measurements).

Conclusion: In summary, we speculated two indications of HP in Covid-19 patients: to modulate the unbalanced inflammatory response and when the immune paralysis promotes a co-infection.

26

Urinary TIMP2*IGFBP7 is An Early Biomarker of Acute Kidney injury and Early Predicts CRRT START in Critically Ill Patients

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Background: Standard criteria for acute kidney injury (AKI), like serum creatinine (sCr) and urine output (UO), are poor, late and non-specific diagnostic tools, measuring renal function, but not renal injury. The Objective of the study was to analyze tissue inhibitor metalloproteinase-2 (TIMP2) * IGF-binding protein 7 (IGFBP-7) for early prediction of AKI, evaluating its role to start precociously the continuous renal replacement therapy (CRRT)

Methods: Observational study enrolling 42 patients after cardiac surgery. TIMP-2*IGFBP7 was examined in serial urine collections pre-surgery (T0), at ICU admission (T1), after 24 (T2), 48 (T3) and 72 h (T4).

Results: TIMP-2*IGFBP7 was defined as “positive for AKI” at a concentration >1.6 (ng/ml)² /1000. We performed a ROC curve to evaluate the predictive ability of [TIMP-2].[IGFBP7] for AKI: [TIMP-2]*[IGFBP7] showed the best performance for severe AKI (stages 3) at 24 hours (T1): AUC 0.78 (95%CI 0.66–0.82). Moreover, the CRRT treatment duration was significantly longer in patients who had a TIMP-2*IGFBP7 concentration > 1.7 (ng/ml)² /1000 at T1 (6.7 ± 1.3 days versus 4.2 ± 1.1 days. $p=0.02$).

Conclusion: Early assessment of TIMP2*IGFBP7 after admission in ICU (T1) may predict severe AKI, allowing for precocious start of RRT in patients with normal serum creatinine and urinary output. However, this biomarker could be inserted in a clinical score (SOFA, APACHE) not evaluating a single value, but its trend during the first 3 days of ICU stay.

Covid19, Pneumococcus, Sickle Cell Disease and Microangiopathy in an infant: A Case Report of the Perfect Storm Successfully Treated by CRRT

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A previously healthy Nigerian 20-months-old girl presented to the emergency department in critical clinical condition with fever, hypotonia and lethargy.

Lab tests showed hypoglycaemia with metabolic acidosis and normocytic anaemia, with normal white blood cell and platelet count. The C-reactive protein (CRP) level was 12.8 mg/L (nv <5 mg/ml), procalcitonin levels were high (50 ng/ml, nv <0.5 ng/ml). Thus, she received glucose solution, a dose of ceftriaxone, a red blood cell transfusion and a haemoculture was collected. The child tested positive for SARS-CoV-2 nasopharyngeal swab.

In a few hours her clinical conditions worsened with significant respiratory distress that required mechanical ventilation and admission to ICU. Chest X-ray showed interstitial infiltrates with no consolidation. Sars-Cov-2 was confirmed on BAL.

At re-evaluation her inflammatory markers were skyrocketing (PCT 400ng/ml, PCR 37 mg/dl, WBC 18080/mm³). Therapy with meropenem, vancomycin and immunoglobulins was started.

Laboratory tests showed a severe thrombotic microangiopathy (haemolytic anaemia with dropping Hb (5.9 g/dl) and platelet count (18.000/ul), undetectable haptoglobin, high LDH levels) with concomitant fulminant hepatic failure. Haemoculture was positive for *S. Pneumoniae*. The blood smear showed sickled red cells, Hb electrophoresis showed HbS presence and genetic analysis confirmed the diagnosis of sickle cell disease.

The child's conditions kept worsening and, after a few hours, she developed anuria with increased creatinine levels, severe acidosis and a rapidly worsening fluid overload and capillary leak syndrome.

Facing the diagnosis of sepsis and the multifactorial thrombotic microangiopathy secondary to SARS-Cov-2, sepsis and sickling crisis, continuous renal replacement therapy (CRRT) as continuous veno-venous hemodiafiltration was started choosing citrate anticoagulation, due to extremely altered coagulation asset with a Prisma[®] HF20 device (Qb 70 ml/min, PBP 700 ml/h, Dialysate 1000 ml/h, Replacement 700 ml/h, Calcium compensation Ca 130% for persistent hypocalcemia).

CRRT was performed for 24 hours then the coagulation of the circuit required the circuit substitution with a ST60 and heparin anticoagulation due to the prevailing thrombotic diathesis developed for the sickling crisis.

CRRT was maintained 36 hours and then interrupted with the reverting of the metabolic acidosis, diuresis reprisal and hemodynamic stabilization. Mechanical ventilation was discontinued on day 11th and the child discharged from the ICU after 18 days in improving conditions, normalized renal function and complete resolution of the systemic involvement.

The coexistence of three potential causes of thrombotic microangiopathy made the diagnosis and the initial treatment challenging and the prompt start of CRRT allowed a good control of both fluids and the inflammatory cascade.

influence of CRRT on Acute Kidney injury: A Strange Case of H1N1

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Background: Renal impairment in multiple myeloma in 10% of cases requires replacement dialysis treatment. We evaluated the effect of hemodialysis methods involving endogenous reinfusion (HFR Supra) on the removal of circulating light chains in a patient suffering from multiple myeloma and Acute kidney injury (AKI).

Introduction: 72-year-old male patient with multiple myeloma was hospitalized for H1N1 influenza pneumonia and AKI on pre-existing CKD.

Methods: After three days from diagnosis, despite the antiviral therapy, there was a sudden clinical worsening with oligo-anuria; therefore, it was necessary to start dialysis after the placement of a central venous catheter. We continued with 23 intermittent hemodialysis treatments in HFR Supra mode for the removal of circulating light chains. The patient continued the replacement hemodialysis treatment in HFR mode.

Results: Serum immunoglobulin light chain values were used as control markers of disease progression: Igk, Igl and ratio Igk/Igl (R k/l). At the time of the diagnosis of medullary plasmacytoma the following concentrations were found: Igk was 15,2 g/L, Igl was 0,3 g/L; R was k/l 50,67. After the 10 HFR Supra hemodialysis treatments, those values were decreased: Igk 7,04 g/L, Igl 0,22 g/L with a R k/l of 31,29.

Conclusion: The therapeutic strategy is based on the attempt to reduce the blood concentration with HFR Supra. The decrease of Igk and Igl light chains, detected after HFR Supra cycles, was correlated with a stability of the patient's general clinical condition. Removing the circulating light chains in a patient with multiple myeloma would be useful not only in terms of slowing the progression of the disease and of the consequent organ damage associated with it, but also it can be useful for increasing his/her survival.

Continuous Renal Replacement Therapy with Cytosorb in a Polytrauma Patient - When to Start?

A Case Report

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Background: Polytrauma is one of the leading causes of death in the young population. The most common causes of late death in those patients are septic complications and multi-organ failure. We evaluated use of continuous renal replacement therapy (CRRT) with Cytosorb haemoadsorber and with Oxiris adsorptive membrane in treatment of acute renal injury (AKI) caused by rhabdomyolysis. The focus was on optimal timing for initiation of CRRT.

Table 1. Values at admission, before and after CRRT

	ICU admission	2 nd Day Before CRRT	4 th Day After CRRT
Interleukin 6 (pg/ml)	–	599.4	361.2
C-reactive protein (mg/l)	1.8	125.5	214.9
Procalcitonin (ng/ml)	4.18	135.0	63.35
White blood cells count (10 ⁹ /l)	27.86	11.15	7.34
pH	7.24	7.27	7.50
Lactate (mmol/l)	3.41	3.73	2.19
Urea (mmol/l)	5.3	14.7	10.0
Creatinine (µmol/l)	143.00	400.00	305.00
Potassium (mmol/l)	6.88	7.50	3.79
Norepinephrine (µg/kg/min)	1.1	0.6	0.15
ALT (u/l)	168	482	393
AST (u/l)	417	2355	1561
CK (ng/ml)	1380.7	1140.0	1024.6
SAPS II	68	80	90
APACHE II	30	35	60
MAP (mmHg)	67	76	58

Legend: ALT - alanine aminotransferase, AST - aspartate aminotransferase, CK - creatine kinase, SAPS - simplified acute physiology score, APACHE - acute physiology and chronic health evaluation, MAP - mean arteriale pressure

Methods: A 31-years-old man, without comorbidities was admitted at Intensive care unit with severe polytrauma (head injuries, thoracic trauma, multiple fractures). He was haemodynamically unstable, sustained by norepinephrine infusion, septic, with respiratory failure requiring invasive mechanical ventilation, APACHE II score was 30 and Glasgow Coma Scale Score was 3. AKI was diagnosed at the admission, caused by haemorrhagic shock and crush syndrome. On the 2nd day was started CRRT with regional citrate anticoagulation. We performed two procedures of continuous venovenous haemodiafiltration (Qb 150 ml/min, Qd 1200 ml/h, Qrpre 2000 ml/h, Qrpost 500 ml/h, dialysis dose 40 ml/kg/h). First one was with CytoSorb haemoadsorber and the second procedure with Oxiris adsorptive membrane (Gambro, AN-69, based membrane, surface treated by polyethylenimine and grafted with heparin). Decline of pro-inflammatory markers and improvement of kidney and liver function was noticed after procedures. Despite all efforts of resuscitation patient died on the 6th day of hospitalisation.

Results: Values of pro-inflammatory, kidney and liver markers, blood gas analysis, vasopressor dose before and after CRRT with use of haemoadsorber and adsorptive membrane are presented in Table 1.

Conclusion: Insufficient response to the treatment indirectly indicates the importance of early initiation of CRRT, within 12–24 h of diagnosis of AKI. It also indicates that lowering the cut off values of procalcitonin, Interleukin-6 and APACHE II score before treatment with Cytosorb should be considered.

30

Mortality in COVID19 Patients Underwent to CRRT

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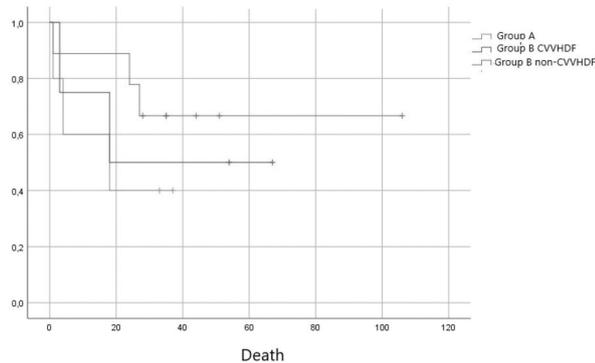
Background: Covid-19 is most popular infection of this year. Its pathogenesis is due to Sars-Cov- 2, a virus of *Orthocoronavirinae*'s subfamily. First known symptoms was an interstitial pulmonary disease but other organs may be affected as kidney with Acute Kidney Injury (AKI). We decided to evaluate patients admitted to ward of intensive care of University Hospital "G. Martino" of Messina.

Methods and Patients: we included in our study all patients admitted to ward of intensive care of University Hospital "G. Martino" of Messina with positive Covid19 test. We used **Chi-Square test with Fisher Test** for dicotomic variables and **T-student test** or **Mann-Whitney test** for continue variables. We used **Kaplan-Meier test** to evaluate patient's survival. Then, we studied in Group B the differences in outcomes between CVVHD treatment and non-dialytic treatment.

Results: Tab 1 summarized basal feature of whole sample. 12 patients have had an episode of AKI. We split our sample in two groups: Group A (6 patients without episodes of AKI) and Group B (12 patients with at least 1 episode of AKI). There are not differences

Table 1.

Age	66,72	±14,14
GFR	65,89	±39,46
Hb	11,48	±2,72
WBC	11341	±5345
Htc	33,7	±9,35
PLT	202875	±95934
Blood urea	89,25	±63,76
LDH	1113	±672
CPK	774	±1140
Na	137,7	±10,01
K	4,33	±0,6
Ca	7,82	±0,78
Myoglobin	429	[1379,50-91,50]
PCR	17,7	12,91
IL6	84,6	[185-52]
D-Dimer	2.69	[1,51-4]



between Group A and Group B in these features. All patients needed CRRT were treated with CVVHDF mode. CVVHDF patients have not a shorter hospital stay compared to non-dialytic treatment.

There are not differences of mortality neither between Group A and Group B neither between Group with CVVHDF treatment and non CVVHDF treatment, with a tendency to best survival to AKI patients compared to non-AKI patients (Fig1).

Conclusion: Despite the worst clinical condition, mortality in patients underwent to CRRT is not worst then other patients.

31

AKI: Cause O or Consequence of Tsunami COVID-19?

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Background: Acute Renal Failure (AKI) occurs in 0,5-23% COVID-19 patients during hospitalization. In these patients, the principle of carrying out CRRT using the CytoSorb adsorbent cartridge lasting 24 hours is based on the role that pro-inflammatory cytokines play in the pathogenesis of Acute Respiratory distress syndrome (ARDS).

Introduction: A 59-year-old male COVID 19 patient suffering from dysthyroidism and Hypertension, was admitted to the Intensive Care Unit (ICU) for ARDS. Laboratory test showed: serum creatinine of 2.27 mg / dl with eGFR 30 ml / min CKD-Epi, anemia, thrombocytopenia and lymphopenic leukocytosis.

Methods: After 1 month from the beginning of his hospitalization, an oligoanuric AKI led to the start of Continuous renal replacement therapy (CRRT) lasting 24 h using Continuous Hemodiafiltration (CVVHDF) cartridge via left jugular with a subsequent clinical improvement and of an adequate diuresis.

After three days from the last hemodialysis treatment, the patient complained of abdominal pain in the right hypochondrium: he was treated with empirical antibiotic therapy after Computed Tomography (CT) examination.

Results: during the hospitalization, an alteration of renal function indices was recorded, although an adequate diuresis with a negative water balance was detected with oral diuretic therapy. The laboratory, radiological and clinical data were suggestive of "acute cholecystitis"; thus, the patient was cholecystectomized in hemodynamically stable conditions, thank to the previous extracorporeal dialysis treatments. .

Conclusions: In the postoperative period, the patient did not present post-procedural complications or need for further hemodialysis treatments; instead, he had a Progressive increase of the eGFR. On admission, serum creatinine and eGFR values showed an improvement in renal function (serum creatinine: 1.54 mg / dl; eGFR: 49 ml / min). This case suggests the validity of Continuous Hemodiafiltration for the treatment for oligo-anuric AKI in Sars-CoV-2 infection.

32

Role of D-DIMER as Predictive Factor of COVID-19 Severity: An Observational Study in a Single institution in Lombardy, Norther Italy

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Background: The intent of this work is to describe the observations collected during the treatment of SARS-CoV-2 patients carried out by our ICU (Intensive Care Unit) in the months of February to May.

Methods: This is a descriptive work on the clinical, biochemical and ventilatory characteristics of patients at the time of hospitalization in ICU, after 3 and 5 days. In intubated patients, the Ventilatory Ratio (VR) was used for the indirect assessment of dead ventilatory space.

Results: We evaluated 76 patients; we underline that 82% of patients are men with an average age of 62. At the entry into ICU the mean blood D-dimer level was similar in the two groups of patients considered, with Pvalue 0.238. The determination of the VR in all patients undergoing mechanical ventilation demonstrates a substantial difference between surviving patients, with mean value 1.01 (SD 0.47) and deceased, with 1.32 (SD 0.45 Pvalue <0.01).

Discussion: We observed a direct relationship between the dosage of D-dimer at the time of patient admission to ICU and the patient's ICU hospitalization time with respect to mortality R2 0.246; F (1.18), Pvalue 0.026. The data of the increased level of fibrinolysis led us to try to indirectly determine the amount of ventilation not used for respiratory exchanges and therefore wasted as dead space. The method chosen was the determination of the VR with which it was possible to observe an increase of about 30% in the minute ventilation necessary to maintain in the physiological range the arterial carbon dioxide level in the deceased patients. The VR of the survivors is around 1.01 (SD 0.467) while the VR of the deceased is around 1.32 (SD 0.455) with R2 0.104 (Pvalue 0.006).

Conclusions: We can therefore assume that careful monitoring of the D-dimer (examination with low economic impact and which can be performed routinely) and its correlation with the time of hospitalization in a non-intensive environment allows us to recognize patients with greater impairment of ventilation / pulmonary perfusion and increased dead space.

33

IgA Monoclonal Gammopathy: An Uncommon Cause of High Anion Gap Metabolic Acidosis. A Case Report

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Background: Metabolic acidosis is frequently encountered in emergency settings. It may recognize many different causes. Here, we report an uncommon case of severe high anion gap (AG) metabolic acidosis associated with a monoclonal gammopathy of renal significance (MGRS) due to monotypic IgA deposits.

Case Presentation: A 58-year-old woman was admitted to the emergency room for acute dyspnea. Hemodynamic parameters were normal, but ABG showed extremely severe metabolic acidosis with hyperkalemia and elevated anion gap (pH 6.9, pCO₂ 9 mmHg, Bic 1.9 mmol/L, pO₂ 111 mmHg, K+ 6.2 mmol/L, Cl 109 mmol/L, Ca⁺⁺ 1.21 mmol/L, Lac 1.8 mmol/L, AG 32). Lab exams also showed severe acute kidney injury (creatinine 20.4 mg/dL vs previous value 2.5 mg/dL) and severe anemia (Hb 6.4 mg/dL), while glucose and other metabolic parameters were normal. She had no history of diabetes, hypertension, or other illness. The patient

denied diarrhea or drugs intake. Because of rapidly worsening dyspnea, mechanical ventilation was started. In the meanwhile, CVVHD treatment was initiated and continued for 4 days, when it became possible to withdraw dialysis. Then, the patient was transferred to the nephrology ward, because of persistent severe renal failure (creatinine 6.0 mg/dL). Laboratory examinations showed increased IgA circulating levels (5 g/L). A renal biopsy resulted in the diagnosis of monotypic immunoglobulin IgA lambda deposition disease (bone marrow biopsy was negative for myeloma). Then, therapy with Dexamethasone and Bortezomib was started with the progressive recovery of the renal function (two months after creatinine was 2.5 mg/dL, eGFR 20 mL/min). The patient is still in follow-up; the renal function is stable and ABG normal.

Conclusion: High anion gap acidosis is potentially associated with IgA gammopathy. Indeed, it has been proved that IgA paraproteins (in particular IgA lambda chains), having an isoelectric point slightly below physiologic pH, may act as anions in the serum. So, monoclonal gammopathies should be included in the diagnostic workup of unexplained metabolic acidosis.

34

Hemoperfusion Experience in SARS-COV-2 Patients

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Objective: Demonstrate that Hemoperfusion (HP) is effective to relieve the covid-19 Hyperinflammatory syndrome (cHIS). To evaluate the role of convective and adsorptive therapies as organ support in COVID-19 patients. Compare the effectiveness of continuous (CHP) vs intermittent (IHP).

Method: Cohort prospective study in 24n COVID-19 critical ill patients. IHP (JAFRON HA 330 cartridge) 2-1-1 scheme was used and CHP scheme consisted of 48h treatment (CYTOSORB cartridge), 24h each one. The outcomes were IL-6, ferritin, LDH, D-Dimmer, lymphocyte seric levels pre and post intervention and finally mortality. T-student test was developed for median difference. Therefore length of ICU stay, ventilation mechanical and vasoactive drugs dependence were analyzed. In AKI patients who start continuous renal replacement therapy (CRRT), the dialytic modality and prescribed dose was continuous venovenous hemodiafiltration (CVVHDF) 35 ml / kg / h with HP on series.

Results: Age mean 65y, MCI 30,21 (SD 4,5) CALL score 9,96 (SD 2,25), SOFA mean 11,7 (SD 1,8), Mellitus Diabetes 25%, Cardiovascular disease 41,7%, Chronic Respiratory Diseases 4%, Neoplasia 4%. Comparing IHP group vs CHP the IL-6 mean decrease 60% vs 29% (p=0,003), Ferritin decrease 33% vs 29%; LDH 32% vs 2%. All patients met criteria for cHIS, The total mortality was 42,8% (IHP 38%) (CHP 50%)

Conclusion: Based on SARS-CoV-2 pathophysiology, a rationale emerges for HP in order to remove inflammatory mediators; The HP efficacy to combat cytokine storm is better evidenced with intermittent HP than continuous HP. The mortality is understandably high in critically ill patients with severe mortality scores.

However the results are encouraging and apparently show more efficiency in Intermittent HP technique.

35

Hemoperfusion in ERC5D Patient with Sepsis Table due to Acute interstitial Pneumonia Secondary to SARS VOC 19 infection - Case Report

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Background: Adsorption techniques have proven useful in the management of chronic and / or acute kidney patients. The most important stage is sepsis where it acts as an adjuvant in the immunomodulation process of the systemic inflammatory response (SIRS). In these cases, hemoperfusion provides benefits in balancing said response.

The SARS COV 2 (COVID19) infection produces in some patients an intense SIRS called cytokine storm, which casts a shadow on patient survival.

Method: A case of a 66-year-old CKD5D woman is reported secondary to diabetic nephropathy presenting with symptoms of acute respiratory failure associated with fever and SIRS with rapid IgM (+) test for COVID 19 and tomographic findings compatible with atypical interstitial pneumonia. SCORE APACHE II and SOFA are calculated, establishing criteria for sepsis and mortality of around 15%. It was decided to undergo conventional hemodialysis therapy with a polyethersulfone (PES) filter plus hemoperfusion with a HA330 Disposable Hepmoperfusion Cartridge filter.

Results: Baseline values: ECG: 10 / 15pts, APACHE II 18 pts, SOFA 6, PaFiO₂: 240 mmHg, procalcitonin 10ng / ml, CRP 3.1mg / L, leukocytes 9290 cells / mm³. The patient received only 2 hemoperfusion sessions applied on consecutive days, each lasting 3 hours, after which the following were observed: ECG: 13/15 pts, APACHE II 16, SOFA 5, PaFiO₂: 342 mmHg, procalcitonin 0.3ng / ml, CRP 0.1mg / L, leukocytes 5200 cells / mm³.

Conclusion: There was clinical and laboratory improvement after the application of the haemoperfusion sessions, which suggests that their use benefits the evolution and prognosis of septic symptoms secondary to atypical respiratory infection.

36

Potential Role of Pancreatic Stone Protein (Psp) as Early Marker of Bacterial infection in Covid-19 Patients

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Background: Sepsis is a life-threatening condition that needs immediate diagnosis and treatment to maximize the chances of survival. Bacterial sovrainfection is a severe and frequent complication among COVID-19 patients and its diagnosis is challenging. Previous reports suggested that Pancreatic Stone Protein (PSP) may be a sensitive marker for detection of sepsis in critically ill patients. We report a case series of three COVID-19 patients admitted to our intensive care unit (ICU) that were diagnosed with sepsis and received daily monitoring of PSP levels.

Methods: We monitorized PSP, procalcitonin (PCT), and C-reactive protein (CRP) levels in three COVID-19 patients admitted to our ICU between the 26 of August and the 14 of October 2020. Microbiological sampling and antibiotic treatment were performed according to the ward organization and whenever a clinical suspect for infection was present. Positive cultures and antibiotic treatment were retrieved from clinical charts. Patients were followed from the day of ICU admission up to a maximum of 20 days.

Results: Patient 1 was a male, age 55 years, overweight with no other comorbidity. He was admitted to the ICU with non-invasive ventilation and was already undergoing treatment with Ceftriaxone that was interrupted on day 7. On day 2 he was intubated. Piperacillin/tazobactam was started on day 12 for suspected hospital acquired pneumonia. PSP levels markedly increased on day 10 with no significant changes in CRP and PCT levels. Bronchospirate was performed on day 13 with isolation of *Klebsiella pneumoniae* with CFU > 10⁶ (Figure). Patient 2 was a 70 years old man, with mild emphysema and diabetes. At ICU admission PSP level was 287 ng/ml and he was not receiving antibiotic treatment. His conditions rapidly worsened requiring intubation and characterized by the development of a severe septic shock (Figure). CRP levels markedly raised between 48 and 72 hours after the detection of increased PSP with only mild increase of PCT. Patient 3 was a male, 78 years old without comorbidities. Similarly to patient 2, on the day of ICU admission PSP level was elevated and he was receiving piperacillin/tazobactam. After 48-72 hours, CRP levels increased with no significant changes of PCT. Endotracheal aspirate was collected on day 3 and it was positive for *Ps. aeruginosa* (Figure).

Conclusion: Our findings suggest a potential role of PSP as early marker of sepsis in critically ill COVID-19 patients. Daily PSP monitoring may anticipate the inception of an appropriate treatment in COVID-19 patients with a septic complication in comparison with the actual laboratory markers. Further studies are needed to confirm our hypothesis.

Epidemiology of Acute Kidney injury in not ICU Admitted Patients for COVID-19 infection

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Background: COVID-19 is a systemic disease that involves the kidney since SARS-CoV-2 has a high kidney tropism. The aim of this study was to describe the epidemiology, risk factors and outcomes of acute kidney injury (AKI) in patients hospitalized for Covid-19 in a General Medicine COVID-Units. Critically ill patients requiring mechanical ventilation were excluded because our aim was to evaluate virus-related kidney damage without intubation sequelae.

Methods: A retrospective cohort study was performed on all patients hospitalized for COVID-19 in Pavia San Matteo Hospital COVID-Units from March 2020 until June 2020. AKI was diagnosed according to KDIGO 2012 guidelines and patients were categorized as having pre-renal or renal AKI if FENa was < 1% or >1%. Community-acquired AKI (CA-AKI) was defined as patients whose admission serum creatinine met KDIGO criteria, while hospital-acquired AKI (HA-AKI) was defined as an increase in serum creatinine that occurred twenty-four hours or longer after hospitalization. Demographic, laboratory and clinical outcome variables were extracted by chart review.

Results. AKI was diagnosed in 54 on 253 hospitalized patients (21,3%) and prevalent in males (M/F ratio: AKI vs not-AKI 2.8 vs 1.4. $p < 0.001$) and older patients (AKI vs Not-AKI 76.23y vs 71.1y $p < 0.05$). CA-AKI was prevalent (55.56%) and renal AKI was more common in both groups. Hospital mortality was higher in AKI group (AKI vs not AKI: 51.8 % vs 21.7% $p < 0.0001$).

Age, previous CKD, obesity, male sex, high flux ventilation and treatment with vancomycin contributed significantly to AKI in the Cox regression model.

Covid-19 infection is associated with pathologic urinalysis in most patients: microhematuria (62%), leukocyturia (44%) and abnormal UACR (85%). Only 13% of these patients had AKI.

Conclusion. AKI is a common and serious complication of COVID-19 infection. Renal CA-AKI is the prevalent form. Pathologic urinalysis is frequent and independently of AKI.

Re-Explore the Role of Artificial Liver Support System (ALSS) during COVID-19 Pandemic

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Background: Coronavirus Disease-19 (COVID-19) had been declared as pandemic since 11 March 2020 and there was an exponential increase of cases in Malaysia since mid-March 2020. The outbreak had inflicted major disruption in the healthcare service and transplantation had been suspended temporarily due to logistic reasons and scarcity of resources. To date, liver transplantation is the only effective therapeutic option with proven survival benefits in irreversible acute liver failure (ALF). We would like to report the application of ALSS as bridging therapy in 2 patients with ALF during the interruption of transplantation service due to the pandemic.

Methods/Case: A 24-year-old lady was admitted for ALF due to anti-tuberculosis agents which were started for tuberculosis lymphadenitis. She was intubated for airway protection as encephalopathy ensued with multiple episodes of seizures. Her MELD score was 37 and we could not facilitate the liver transplantation from the other centre due to the pandemic. Haemoperfusion (Jafron HA330-II) was initiated and showed biochemical improvement but nothing from the clinical aspect (Bilirubin 312 to 240 $\mu\text{mol/l}$, Interleukin-6 (IL-6) 208.5 to 92.3 pg/ml). Subsequently, single pass albumin dialysis (albumin 2% with dialysate flow rate of 700mL/hour) was attempted but was withdrawn due to severe coagulopathy and she succumbed secondary to hospital acquired infection.

1. A 26-year-old indian citizen was admitted for ALF secondary to alcoholic hepatitis with a MELD Score of 40. He was monitored closely while the family was arranging for the medevac service back to India for liver transplantation. The transfer required intricate legal documentation during the pandemic and we had started 3 cycles of haemoperfusion to buy time. We were able to wean off his inotropic support with stabilization of liver parameters before his transfer (Bilirubin 619 to 461 $\mu\text{mol/l}$, Ammonia 92 to 57 $\mu\text{mol/l}$).

Conclusion: ALSS can be employed as one of the therapeutic options as bridging therapy while waiting for liver transplantation especially during this pandemic. However, patient selection and the appropriate timing for initiation warrants future study.

Procalcitonin and C-reactive Protein as Mortality Predictors in Sepsis-induced Acute Kidney Injury

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Introduction/Objective: Acute kidney injury (AKI) is a frequent and serious sepsis-induced complication in patients in Intensive care unit (ICU). The objective of this study was to evaluate the prognostic value of C-reactive protein (CRP) and procalcitonin (PCT) as predictors of 28-day mortality in patients with sepsis induced AKI.

Methods: We performed a single-center retrospective study of 440 adult surgical and non-surgical patients with AKI and episode of AKI in chronic kidney disease (CKD) who were admitted to the ICU between 2014-2018 and received Renal Replacement Therapy. The day of confirmed diagnosed AKI, laboratory and clinical parameters were analysed.

Results: Out of 440 patients, 249 (56.60%) survivors had significantly less prevalent CKD, less qSOFA score, and lesser need for vasopressor therapy and mechanical ventilation when compared to the deceased ones. There was a significant difference in CRP value ($p < 0.0454$), but not in PCT value ($p = 0.6735$) between survivors and non-survivors. There were significantly more ($p < 0.0142$) surgical patients in the septic group having a significantly greater ($p < 0.0153$) need for vasopressor therapy. The median CRP and PCT values were significantly higher ($p < 0.001$) in septic patients (183.24 vs 33.21) in comparison with non-septic patients (109.74 vs 13.73). A significantly greater number of

Table 1. Comparison of demographic and clinical parameters between patient groups

	Survivors (n=249)	Non-survivors (n=190)	p	Septic patients (n=205)	Non-septic patients (n=235)	p
	N (%)	N (%)		N (%)	N (%)	
Mean age-years (SD)	61.45 (13.99)	62.57 (12.75)	0.3752	61.89 (13.17)	61.95 (13.74)	0.9625
Female	41 (16.46)	67 (35.07)		70 (34.14)	76 (32.34)	
Male	208 (83.54)	123 (64.93)		135 (65.86)	159 (67.66)	
Surgical patients	74 (29.71)	54 (28.27)	0.3706	80 (34.04)	48 (23.41)	0.0142
qSOFA	0.5662	2.7400	<0.0001	1.6048	1.434042553	0.1432
Urea (mmol)-median (IQR)	26.69	27.41	0.5817	26.4325	27.51	0.3966
Creatinine (µmol)-median (IQR)	396.07	379.65	0.3904	386.2926	391.26	0.7934
Comorbidities N (%)						
CVB	82 (42.93)	107 (42.97)	0.9933	85 (41.46)	104 (44.25)	0.5561
PD	22 (11.51)	36 (14.45)	0.5632	30 (14.63)	28 (11.91)	0.5904
GD	21 (10.99)	34 (13.65)	0.4042	26 (12.68)	29 (12.34)	0.9139
DM	35 (18.32)	35 (18.32)	0.1739	50 (24.39)	44 (18.72)	0.1486
CVD	19 (9.94)	19 (7.63)	0.3922	13 (6.34)	25 (10.63)	0.1099
CKD	4 (2.09)	16 (6.40)	0.0306	9 (4.30)	11 (4.68)	0.8842
Sepsis	108 (43.37)	97 (50.78)	0.1120	97 (47.32)	94 (40.00)	0.1229
Physiological support N (%)						
VT	138 (72.25)	145 (58.23)	0.0022	144 (70.24)	139 (59.14)	0.0153
IMV	136 (54.61)	141 (73.82)	<0.0001	135 (65.85)	142, (60.42)	0.2405

Legend: qSOFA-Quick sepsis related organ failure assessment; CVD-Cardiovascular diseases; PD-Pulmonary diseases; GD-Gastrointestinal diseases; DM-Diabetes mellitus; CVD-Cerebrovascular diseases; CKD-Chronic kidney disease; VT- Vasopressors therapy; IVP-Invasive mechanical ventilation

Table 2. Comparison of CRP and PCT between a groups of patients

	CRP (mg/L) median (IQR)	p	PCT (ng/l) median (IQR)	p
Survivors	133.89	0.0454	21.75	0.6735
Non-survivors	157.15		24.13	
Septic patients	183.24	<0.001	33.21	<0.001
Non-septic patients	109.74		13.73	

Legend: CRP-C reactive protein; PCT-procalcitonin

Table 3. Comparison of cut-off values of CRP and PCT in septic and non-survivors patients

	Septic patients N(%)	p	Non-survivors N(%)	p
CRP <100 mg/L	65 (32.01)	<0.001	84 (41.37)	0.4277
CRP >100 mg/L	140 (59.07)		107 (45.14)	
PCT <10 ng/ml	39 (25.82)	<0.001	90 (59.60)	0.3580
PCT >10 ng/ml	166 (57.43)		159 (55.01)	

Legend: CRP-C reactive protein; PCT-procalcitonin;

patients ($p < 0.001$) had a level of CRP >100mg/L and PCT >10ng/ml (59.07% vs 32.01%) in the septic group in comparison to the patients whose values were CRP <100mg/L and PCT <10ng/ml (57.43% vs 25.82%), but no significant difference was found between the CRP and PCT cut-off values between survivors and non-survivors.

Conclusion: CRP value can be used as mortality predictor in sepsis-induced AKI in critically ill patients. This result indicates the necessary monitoring of CRP and PTC values from the day of admission, the day of diagnosis of sepsis and AKI to the time-defined outcome, taking into account all clinical parameters that affect the dynamics of values.

40

Management of Postoperative Complications and Implications: A Case Study

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Introduction: Postoperative complications contribute to increased mortality, length of stay and need for an increased level of care at discharge. In these complex cases, a multiple organ support therapy might be currently seen as a feasible approach.

Patient case: We present a case of a 71-year-old female who underwent bypass surgery due to CAD. After 6 weeks she was admitted to our clinics due to severe progressing dyspnoe, fatigue and weakness. On primary survey, her general condition was very severe, patient was lying, passive and frail, respiratory rate was 20/min, oxygen saturation of 90% beyond oxygenotherapy; diuresis 300 ml per day, GFR 40 ml/min (by MDRD). HR was 86 bpm, irregular (atrial fibrillation), TA 90/80 mm Hg. Chest CT demonstrated bothsided hydrothorax and right sided atelectasis with infiltration. The patient underwent pleural puncture, cytology of punctate revealed transudate, no malignant cells. Physyterapeutic evaluation reported: functional assessment measure level - complete assistance is necessary, balance disorder by Berg scale accounted 0 points, sitting balance by Leahy was 1 point, Rivermade mobility index 1-3. Management approach included strict fluid balance control, 50 mg Torasemid once a day, activation, verticalization.

Results: After 2 weeks general condition improved - no dyspnoe, TA 130/80 mm Hg, no need of oxygen, diuresis 1700 ml with no diuretics, GFR (by MDRD formula) 81,87 ml/min, functional assessment measure level- modified independent (requires an assistive device), balance disorder by Berg scale 10 points, sitting balance by Leahy - 3, Rivermade mobility index- 4-7.

Conclusions: This case illustrates the prompt and accurate management of MODS and frailty leading to optimal patient outcome.

41

Laboratory Parameters (Procalcitonin, interleukin-6 and CRP) Dynamics during the Treatment with Cytokine Adsorption (HA-330 Adsorber)

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Objective: to evaluate the dynamics of procalcitonin, IL-6 and CRP during the treatment with cytokine adsorption.

Methods: The investigation included COVID-19 patients with multiple organ failure, subtotal lung injury with ARDS and received CRRT due to acute kidney injury. Patients were categorized

into 2 groups according to extracorporeal hemocorrection treatment regimen. The 1st group received conservative therapy, CRRT and 3 hemoadsorption (HA) with cytokine adsorber HA-330. The indication for starting HA was sepsis. The second group received conservative therapy and CRRT. HA regimen with cytokine removal Hemoadsorber – HA-330: duration 6 hours with interval between procedures 12 hours.

Results:

Parameters	Before HA, Median [25 %'s-75 %'s]	HA1, Median [25 %'s-75 %'s]	HA2, Median [25 %'s-75 %'s]	HA3, Median [25 %'s-75 %'s]	P-value (Friedman ANOVA)
Procalcitonin (normal range 0.0–0.5 ng/ml)	3.6 [1.65-33.3]	4.61 [1.38-11.61]	2.33 [1.15-4.2]	0.493 [0.15-1.44]	0.029
IL-6 (normal range 0.0–6.4 pg/ml)	417 [166-980]	155.4 [97.74-281.6]	63.14 [17.61-127]	73.16 [21.96-224.9]	0.04
CRP, mg/dl	21.7 [8.58-125.9]	28.97 [9.84-121.4]	23.2 [11.2-166]	70.5 [10-161.5]	0.42

Comparison of these indicators by Friedman ANOVA showed statistically significant decrease in procalcitonin and IL-6 levels after the 2d HA. After the 3d HA IL-6 slightly increased again. Then 4 groups were compared with each other by Wilcoxon test, which revealed statistically significant decrease in the levels of procalcitonin (p=0.04) and interleukin after 2 hemoadsorption procedures (p=0.04). Changes in the CRP level in both cases remained statistically insignificant.

Conclusions: Therapy with the cytokine adsorber HA-330 showed statistically significant decrease of procalcitonin and IL-6 levels in dynamics after the second procedure. So, it is necessary to consider the issue of continuous cytokine adsorption for the 1st 24 hours or more, possibly in combination with CRRT, since one of the indications for CRRT is an acute respiratory distress syndrome in adults.

42

Clinical Outcomes of COVID-19 Patients Who Underwent Hemoadsorption Therapy

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Background: COVID-19 is an infectious disease caused by the novel coronavirus SARS-CoV-2. Majority of the patients experience mild to moderate disease. Approximately 14% of the patients experience severe disease and 5% develop respiratory failure or

multi-organ failure [1]. No therapy has been shown to conclusively reduce mortality in the critically ill patients.

Methodology: This was a retrospective survey of all patients admitted from March to August 2020 in the critical care unit with confirmed COVID-19 pneumonia who underwent hemoperfusion using HA-330 cartridges therapy. Data regarding the patient characteristics, clinical course of disease and patient outcomes was obtained from the medical records.

Results: A total of 41 COVID-19 patients were admitted to the critical care unit between March to August 2020. 14 (34.1%) patients received hemoadsorption therapy. 12 (85.7%) were males and 2 (14.3%) were females. The mean age was 52.9 years and the median age was 52 years. Majority (78.5%) of the patients had diabetes and systemic arterial hypertension. One patient had a malignancy and 2 patients had asthma and chronic obstructive airway disease. Ten (71.4%) of the patients who underwent hemoadsorption therapy were successfully extubated and discharged from the critical care unit. Three out of the four patients who succumbed had a delay in initiating the hemoadsorption therapy due to delayed consent. One patient who succumbed had progressed well after the hemoadsorption therapy but had a sudden cardiac arrest following an arrhythmia.

Conclusion: Hemoadsorption is a promising modality of treatment for COVID-19 pneumonia with severe acute respiratory distress syndrome. It has to be initiated early to get good clinical outcomes. This is a small retrospective study to draw definitive conclusions from and larger randomized controlled trials are needed to confirm the beneficial effects of this therapy.

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43

Effect of Extracorporeal Hemoperfusion Removal of Inflammatory Mediators and Survival in End Stage Liver Disease Patients with Septic Shock

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Background: To study the effects of HA330 resin cartridge in patients with end stage liver disease presenting to critical care unit with septic shock.

Inclusion criteria: Adult patients presenting within 24 hours of onset septic shock with noradrenaline requirement of more than 10 microgram /min, serum lactate >4mmol/L, APACHE-II Score < 30.

Exclusion criteria: Age < 18 yrs, severe cardiovascular and cranio cerebral disease, severe coagulopathy, severe anemia, active bleeding, long term immunosuppressant therapy, noradrenaline requirement > 0.5mcg/kg/min or requirement of multiple vasopressors.

Methods: Three adult cirrhotic patients admitted to ICU with septic shock matching the inclusion criteria were subjected to hemoperfusion using HA 330 resin cartridge for a duration of 2-4 hrs for three consecutive days using regular dialysis machine. There was no indication for renal replacement therapy in all three patients. Serum levels of IL-6, TNF- α , lactate, dose of vasopressors, APACHE-II score before and after hemoperfusion were measured.

Results: All three patients were weaned off vasopressor dose by day 4 and discharged from ICU by day 5. The IL6, TNF alpha and lactate values decreased following third session of filter. None of the three patients required ventilator support or renal replacement therapy during their ICU stay. Patient 1 had neutropenia and so third filter was not initiated. No other complications were seen as part of hemoadsorption cartridge use. All three patients had gram negative bacterial growth in their blood cultures which was treated with appropriate antibiotics.

Conclusion: HA330 filter effectively removed inflammatory mediators in adult cirrhotic patients with septic shock thereby improving the organ dysfunction and hemodynamic stability and decreased the ICU stay.

44

Hemoperfusion as an Adjuvant Therapy in Severe COVID-19 in Hemodialysis Patients: Experience from Fatmawati General Hospital

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Background: Mortality rate among maintenance hemodialysis (HD) patients with COVID-19 is alarmingly high. In Fatmawati General Hospital, most of HD patients with COVID-19 presented with moderate and severe acute respiratory distress syndrome (ARDS). Hemoperfusion (HP) is a blood purification therapy used to remove cytokines and inflammatory mediators to prevent ARDS and organ failure. Hemoperfusion was performed in HD patients whom have not developed to severe ARDS.

Methods: We report three cases of COVID-19 in maintenance HD patients. HP and HD were performed in two consecutive days when patient developed early ARDS as indicated by inflammatory markers elevation. HD and HP were conducted for 4 hours by using high-flux dialyzer and neutral macroporous resin cartridge HA-330 (Jafron Biomedical Company, China), respectively. All patients received standard of care i.e. anti-viral agent, unfractionated heparin, empirical antibiotic, acetylcysteine, and glucocorticoids.

Result: All three ARDS patients who had HP were subsequently managed without intubation. Case 2 was on high flow nasal cannula while case 1 and 3 were on non-rebreathing oxygen mask. After HP, C-reactive protein (CRP), PaO₂/FiO₂ ratio and chest X-ray were improved. Case 1 and 2 had less dependency to oxygen supplementation and were discharged from the hospital. Case 3 also had improvement after HP but then developed septic shock due bacterial infection few days afterwards and succumbed to the disease.

Conclusion: Improvement in CRP levels, PaO₂/FiO₂ ratio and chest-X ray were observed after two sessions of HP-HD. Based on our clinical experience, timing of HP delivery is crucial and should be performed in early phase of ARDS with early increase of inflammatory marker. This measure may prevent the requirement for intubation in patients with severe COVID-19. Combination use of HP-HD on maintenance HD patients with COVID-19 is promising that merits further investigations.

Keywords: hemodialysis, hemoperfusion, COVID-19, resin, hemoadsorption, cytokine storm

45

Comparison of Death Odds Ratio in Patients with COVID-19 in Groups with Conservative Therapy and after Cytokine Adsorption

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Objective: to determine death risks and odds ratio in patients with COVID-19, multiple organ failure on CRRT and conservative therapy versus treatment by cytokine hemoadsorption (HA).

Methods: The investigation included COVID-19 patients with multiple organ failure, subtotal lung injury with ARDS and received CRRT due to acute kidney injury. Patients with ESRD, oncological and severe somatic pathology in history were excluded from the study. Patients were categorized into 2 groups: group 1 received conservative therapy, CRRT and 3 HA with cytokine adsorber HA-330; group 2 received only conservative therapy and CRRT. There is no statistically significant differences in age, interleukin six and CRP levels in comparing these groups. The indication for starting HA was sepsis. Absolute and relative risks, odds ratio and Fisher exact p (one-tailed, two-tailed) were calculated using 2x2 table.

Results:

Investigated groups	Death	Survivors
HA-330 treatment, n=16	7	9
Comparison group, n=14	10	4

HA-330 vs comparison groups: absolute death risk = 0.29, relative risk = 1.9 and odds ratio = 3.2, Fisher exact p = 0,12 (one-tailed) and 0,16 (two-tailed).

The odds ratio shows that the risk of death is higher in the 2d group compared with the HA group, however obtained data are not statistically significant for this groups.

Conclusions: So, patients treated with cytokine adsorber and CRRT and patients receiving conservative therapy and CRRT had comparable death risk. As obtained data are not statistically significant for this groups, because of small number of patients. More observations are needed to clarify effects of HA on death risk and to for its prevention it is necessary: 1) to develop acute respiratory distress syndrome risk scale, 2) to determine criteria for the earlier start cytokine hemoadsorbition in view of the inflammatory phenotype of the patient, 3) explore HA influence on wider cytokine profile.

46

AKI in COVID-19 Patients

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Background: Several clinical studies have reported that in the course of COVID-19 kidney involvement is not a rarity. In this contest we analysed the blood tests at the hospital admission as potential predictors of AKI in COVID-19 patients.

Methods: The study population encompassed all the 105 patients admitted at the COVID Unit of the A.O.U. Policlinico "G.Martino" between March 8, 2020 and April 27, 2020, with the diagnosis of SARS-CoV2 infection.

Results: Data shown that in our population 33 of 105 patients (29.5%) developed AKI during their hospitalization. The median of AKI onset is 5 days [5.0-6.75]. The maximum timing of development of AKI compared to hospital entrance is 26 days. Table 1 reports the characteristics of the population divided into 2 groups: AKI and No AKI. Kaplan-Meier analysis shown an increase of mortality in patients that developed AKI (p<0.001). We have hypothesized that at the base of the alterations found there was an unbalance of the RAAS. Higher levels of angiotensin II and lower levels of angiotensin 1-7 could be responsible of oxidative stress damage. In addition patients with AKI have higher myoglobin value. Increased myoglobin could be a trigger for renal injury from angiotensin II.

Conclusion: Further studies are also needed to confirm or disprove the possible role of increased angiotensin II and reduction of angiotensin (1-7) in pathogenesis from COVID-19.

Table 1. Baseline characteristic

	No AKI	AKI	p
n	74	31	
Sex, n (%)			0.841
Age, median (min-max)	69 (18–100)	86 (42–92)	<0.001
Chronic kidney disease, n (%)	7 (9.46%)	10 (32.26%)	0.004
Chronic Obstructive bronchopathy, n (%)	2 (2.70%)	5 (16.13%)	0.012
Hemoglobin, (g%)	13.1 (7.4–16.7)	11.8 (8.4–16.9)	0.092
White blood cells (WBC), (mmc)	5700 (2600–13100)	6400 (2200–21200)	0.146
D-dimer, (µg/mL)	0.7 (0.27–4.01)	1.24 (0.31–4.01)	0.011
Creatinine (mg/dL),	0.8 (0.3–2.9)	1.2 (0.4–10.9)	0.003
Azotemia, (mg/dL)	35 (10–117)	62 (18–341)	<0.001
LDH, (U/L)	357 (222–907)	388 (253–1079)	0.249
CPK, (U/L)	64.5 (10–5450)	55 (14–4118)	0.569
Sodium, (mmol/L)	139 (131–153)	144 (136–173)	<0.001
Potassium, (mmol/L)	4.3 (3–5.2)	4.3 (2.7–6.1)	0.626
Myoglobin, (ng/ml)	40 (21–664)	113.5 (30–15000)	<0.001
PCR (mg/dl)	1.5 (0.05–20.8)	3.650 (0.1–30.63)	0.005

47

HA-230 Hemoperfusion Cartridge in the Treatment of Digoxin Toxicity in A 67-Year-Old Male with End-Stage Renal Disease: A Case Report

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Abstract: The HA-230 cartridge is a relatively new and sparsely documented hemoperfusion cartridge that is specifically made to remove excess toxins in the blood using the adsorptive capability of resins to bind to toxins and remove them from the body.

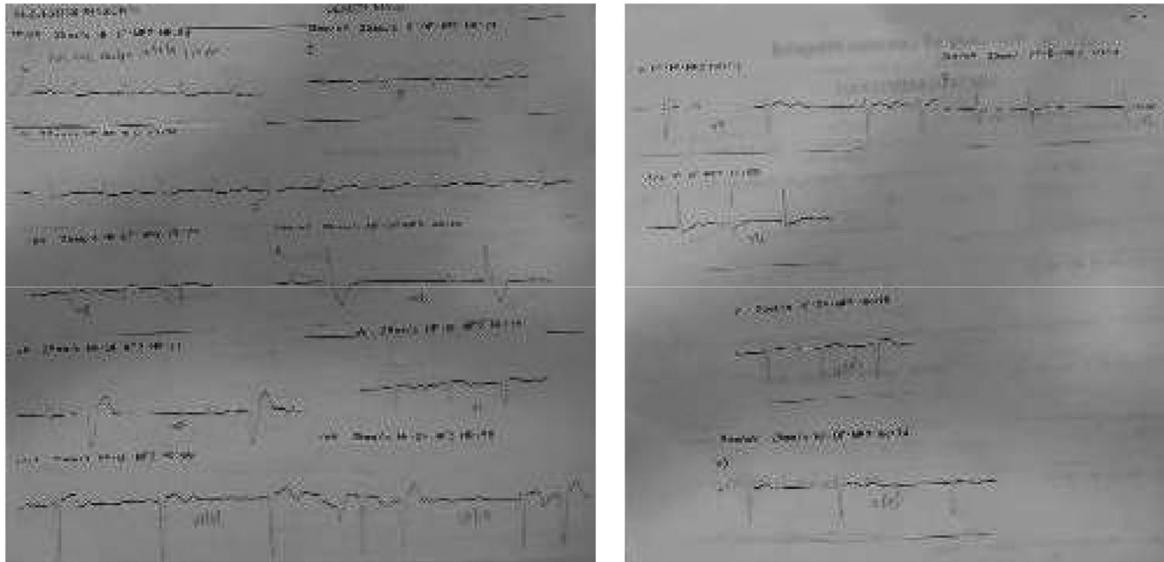


Fig. 1. (ECG–Atrial fibrillation in controlled ventricular response, Occasional ventricular ectopic complexes, Non-specific ST wave changes)

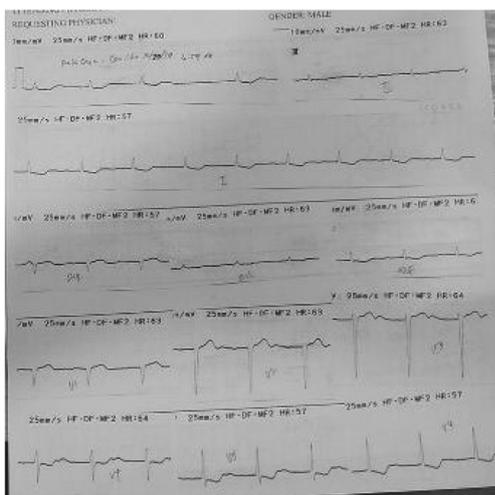


Fig. 2. (ECG post hemoperfusion-Sinus rhythm, First Degree AV block t/c inferolateral ischemia)

Digoxin toxicity is a life threatening condition that may result in arrhythmias when toxic levels are reached, hence in patients with ESRD, care is taken when prescribing these medications. In this case, we report a 67-year old male with ESRD and Heart Failure on Digoxin who was treated as a case of Digoxin toxicity. After undergoing hemoperfusion using the HA-230 cartridge there was noted improvement of patient’s status. The use of this cartridge has shown good promise however, further studies and documentation on its use is still recommended, as there are still only a few documented studies on its use especially in ESRD patients.

Background: Digoxin is a non-dialyzable drug that is part of a drug class called cardiac glycosides. These medications work by inhibiting the Na-K-ATPase within the cardiac myocytes thereby

causing shifts in the intracellular sodium gradient within the muscle. This increase in sodium gradient increases intracellular calcium ions allowing for increased contractility of the myocytes[5]. Additionally, digoxin affects vagal tone, these actions of digoxin can easily cause arrhythmias in patients especially if digoxin levels are at toxic levels[10]. Having a narrow therapeutic range (0.5-1.0ng/ml)[1], digoxin can easily result in toxic or sub-therapeutic levels, hence doses must be adjusted to cater to an individual’s renal function[8]. In patients with End Stage Renal Disease, digoxin use is associated with increased risk for toxicity and subsequently mortality[7]. Hemoperfusion refers to the circulation of anticoagulated blood into an extracorporeal circuit utilizing adsorbent cartridges to remove specific toxins.[9]The HA-230 in particular has a resin pore size of 200 D–10 kD and can remove drugs and toxins of molecular weights of 500 D–10 KD[2]. Clearance of digitalis is therefore possible through hemoperfusion using this cartridge.

Case Presentation: A 67-year-old male, diabetic, hypertensive with heart failure on digoxin, and ESRD on renal replacement therapy and hemodialysis 3x/week came in due to 1 episode of vomiting few hours prior to admission. He reported feeling nauseated during the hemodialysis, which led to an episode of vomiting after the session. This prompted laboratories and ECG to be done revealing normal blood chemistry however ECG revealed sinus bradycardia with poor R wave progression on leads V1-V3 and a mobitz type II heart block. Patient was immediately brought to our institution for observation and evaluation.

At the ER, physical exam revealed rhonchi on both lower lung fields and Grade II bipedal pitting edema. Patient was admitted at the ICU for close monitoring and observation. ECG done at the ER (Fig.1) noted findings of atrial fibrillation in controlled ventricular response with occasional ventricular ectopic complexes, suspecting digoxin toxicity hence, a digoxin serum assay was done.

On the 2nd hospital day, digitalis assay revealed a value of 2.7ng/ml (0.4-2.4), confirming the diagnosis of digoxin toxicity. Patient underwent hemoperfusion with HA-230 cartridge for 3 hours. Patient's status was noted to be steadily improving as documented by the repeat ECG(Fig.2). His repeat digitalis assay after 1 session of hemoperfusion was recorded at 0.5ng/mL. Patient was subsequently discharged on the 4th hospital day and outpatient hemodialysis was continued.

Discussion: In the case above, Digoxin Toxicity was confirmed by the elevated serum digoxin assay of 2.7ng/ml and evidenced by ECG changes and patient's symptoms (nausea, vomiting, bradycardia).

Treatment for patients with digoxin toxicity involves the use of Digitalis immune Fab, this a digoxin specific antibody and a first line drug that specifically binds to digoxin in the body preventing it from binding to its binding site, and allowing the kidney to expel it[1]. However in this patient's case we utilized hemodialysis as well as hemoperfusion using the HA-230 cartridge. The HA-230 is a hemoperfusion cartridge specific for its use on poisoning. It utilizes the adsorptive capability of neutromacroporous resin to remove toxins in the blood.[2,4]

After undergoing hemoperfusion, patient's condition notably improved documented by the ECG, digitalis assay as well as the patient's symptoms.

Shi et. al, (2012), studied the effects of hemoperfusion using the HA-230 in 85 patients with paraquat poisoning. In their study, they noted that the decline in paraquat concentration was greatest in the 1st hour of treatment than the succeeding hours and that higher level of the initial toxin equated to a better response to the treatment. With this they also recommended that frequent therapies might be more effective compared to a single prolonged session of hemoperfusion. This recommendation was echoed by a study done by Hui Dong Et al.(2017). In their study they utilized the use of standard therapy+hemodialysis+hemoperfusion in the treatment of organophosphate poisoning. Their findings showed that frequent therapy showed better cure rates, less atropine use, shorter time of recovery from coma compared to those that did one prolong hemoperfusion session.

Conclusions: This report highlights that use of HA-230 hemoperfusion cartridge in the treatment of a 67-year-old ESRD patient with digoxin toxicity. Patient underwent 1 session of hemoperfusion with HA-230 cartridge and has shown notable progress as evidenced by improvement of symptoms and normalization of ECG.

Recommendations: Further studies of the use of the HA-230 hemoperfusion cartridge is recommended since the utilization of this cartridge is neither widespread nor well documented in the Philippines.

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48

Renal Angina in Critically Ill Patients: Exploratory Analysis of Two Prediction Tools in Fundacion Cardioinfantil in Bogota–Colombia

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Background: AKI implies clinical and economical repercussions. The use of biomarkers economically limited, so is mandatory to use resources wisely, according to worse clinical scenarios through prediction tools that allow selecting patients with higher benefit from interventions to reduce morbidity derived from AKI.

Methods: From our database, we searched adult ICU patients (February- June 2020), excluding those at ICU admission with diagnosis of AKI, serum creatinine >2,5mg/dl, dialysis or kidney transplantation. We evaluate the performance of the Renal Angina Index (RAI), and Acute Kidney Injury Predictor (AKI predictor), to predict severe AKI (KDIGO 2 and 3) at 7 days of follow-up in ICU patients.

Results: A total of 74 patients (72.5%) had severe AKI at 7 days. The ROC AUC for the RAI and AKI predictor score was 0.487 (95% CI 0.363 - 0.61) and 0.62 (95% CI 0.502 -0.737) respectively. A probability of AKI by the AKI predictor tool of 27% or less had a sensitivity of 43.3% and a negative LR of 0.69.

Conclusion: In this exploratory analysis, RAI doesn't discriminate between patients progression risk to severe AKI. An AKI predictor risk lower than 27% suggests that patients won't progress to severe AKI and doesn't require further biomarkers.

Outcomes of AKI With Risk Assessment and Nephrology Rapid Response Team (NRRT) in Adult ICU Patients in Fundación Cardioinfantil in Bogotá – Colombia

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Background: Our ICU protocols adhere to AKI Risk Assessment, we describe AKI outcomes in a colombian ICU with a NRRT.

Methods: From our database, we searched adult patients in ICU (january-june 2020), excluding those at ICU admission with diagnosis of AKI, serum creatinine >2,5mg/dL, dialysis, or kidney transplantation. We reviewed AKI criteria (urine output and creatinine) to establish the incidence of AKI in our ICU and outcomes at discharge under NRRT.

Results: From 881 ICU patients, we included 102 patients with inclusion criteria (women 49%), mean age 58,9 (18-95). Main indication for ICU admission was cardiovascular and mean time in ICU was 5,5 days.

AKI developed in 68% of patients (male 84,6%). Mean creatinine at admission was not statistically different in patients with AKI (0.95 mg/dL; 0.4 -1.80). Sepsis was present in 19,6% of all patients (n 20), and more prevalent in AKI patients (60%, n 12).

CRRT was performed in 2 patients (2%, one deceased, one with renal recovery) and PD in 1 patient (1%, remained in RRT).

Mortality was 6,9% (n 7) mostly in AKI group: (57%, n 4). Mortality was 5,7% of total AKI patients. Vast majority was discharged from ICU.

Conclusion: In our population, AKI is frequently found, but requirement of RRT is low as result of oportune interventions to aminorate kidney injury in ICU.

Effective Discontinuation of Continuous Kidney Replacement Therapy in ICU: The Emerging Role of Cell Cycle Arrest Biomarkers

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Background: Cell cycle arrest biomarkers (CCAB) as TIMP-2*IGFBP7 are elevated in acute kidney stress and can predict the probability of developing acute kidney injury (AKI). However, the CCAB significance to predict renal recovery or successful discontinuation of continuous kidney replacement therapy (CKRT) is unknown. Urine output is the clinical parameter more reliable to expect successful discontinuation of CKRT. The working hypothesis of the present study is: ¿Can the CCAB predict the effective discontinuation of CKRT in critically ill patients?.

Methods: We performed a retrospective single-centre cohort study of patients treated with CKRT, between 2017 to 2019 in an intensive care unit (ICU) of an Italian hospital. Clinical characteristics on admission, in the day of CKRT initiation and the day before the CKRT discontinuation, were collected. CCAB was measured at the admission and discontinuation times. Factors associated with effective discontinuation were identified by binary logistic regression.

Results: Forty-six patients were analyzed, 34 (73,9%) in the effective discontinuation group. UO in mL/kg/h (OR: 9.45, *p*: 0.010) was associated with an increased likelihood of exhibiting effective discontinuation (AUC: 0.75; 95%CI: 0.58-0.92). When, we included CCAB at the admission in the model: UO in mL/kg/h (OR: 7.88, *p*: 0.031) was associated with an increased likelihood of effective discontinuation and CCAB in (ng/ml)²/1000 at enrollment (OR: 0.56, *p*: 0.049) was related with a reduction in the likelihood (AUC of the model 0.86; 95%CI: 0.73-0.99). On the other hand, when we included CCAB collected at the discontinuation: UO in mL/kg/h (OR:8.55, *p*: 0.020) and CCBA in (ng/ml)²/1000 (OR: 0.60, *p*: 0.038) the AUC of the model increased AUC 0.82 (0.61 – 0.99).

Conclusion: Urine output could be a significant factor related to effective discontinuation. However, the addition of CCAB at the admission or discontinuation times can increase the likelihood of successful weaning from CKRT. Further studies are required to confirm our hypothesis.

A Case of Acute Renal Injury After Arteriosclerosis Obliterans Operation Treated by Blood Purification

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Objective: To evaluate the efficacy of blood purification therapy in patients with acute kidney injury (AKI) after recanalization of lower limb arteriosclerosis obliterans.

Method: A 55-year-old male presented with intermittent claudication of both lower limbs for 20 years, aggravated for more than 2 months, and was diagnosed with lower limb arteriosclerosis obliterans (ASO). On June 24, the patient underwent "abdominal aortofemoral artery bypass + femoral arterioplasty + lower limb arteriography" under general anesthesia, and was given blood purification treatment due to acute renal impairment caused by ischemia-reperfusion injury after operation. The decision was made to perform a hemoperfusion and hemofiltration treatment, JaFron HA380 of hemoperfutor and Baxter M150 of hemofilter. The changes of myoglobin, creatinine, urine volume, urine color and inflammatory factors before and after treatment were recorded and compared.

Results: On the first postoperative day, Mb > 2000 ug/l; urine output: 30-50ml/h; urine color was normal; Cre: 248 mmol/l. After 6 hours of hemoperfusion (HP) treatment, Mb: 1800 ug/l, urine volume: 50-80 ml/h. On the second postoperative day, Mb > 2000 ug/l; urine output: 30-50 ml/h, dark urine with soy sauce color, Cre: 340 mmol/l. Blood purification was continued, which was stopped after 6 hours of perfusion, followed by filtration therapy, HP once daily for 6 hours, until myoglobin was less than 2000 ug/l and creatinine was no longer elevated. On July 1, the patient had normal hemogram, decreased inflammatory factors, Mb: 1700 ug/l, urine volume > 200 ml/d, normal urine color, Cre < 200 mmol/l. Blood purification treatment was stopped.

Conclusion: 1. The damage of ischemia-reperfusion to distant organs should be fully assessed, and staged surgery can be considered for chronic ischemia to reduce the risk of AKI; 2. Postoperative urine volume, urine color, myoglobin and other indicators should be closely monitored, once every 4-6 hours, early intervention should be performed to prevent further progression of the disease; 3. Once the occurrence of AKI is determined, blood purification treatment should be performed as soon as possible to remove harmful substances and prevent irreversible renal impairment; 4. Appropriately increase the frequency of hemoperfusion according to the patient's condition and be long in time.

Effectiveness of DPMAS in Supporting Treatment for Acute Liver Failure Patients in Vietnam

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Objective: to evaluate the clinical and subclinical results of double plasma molecular absorption system (DPMAS) as a supporting treatment for patients with acute liver failure.

Patients and method: a prospective non-controlled interventional study was carried out on 27 patients diagnosed acute liver failure (ALF) or acute-on-chronic liver failure (ACLF) from June 2019 to August 2020 with 51 DPMAS episodes at Emergency Department, Bach Mai Hospital. Clinical and subclinical parameters were recorded at admission, before and after each DPMAS episode, mortality rate was collected within 30 days.

Results: Among 27 patients, the male accounted for 88.9%, the mean age was 52.3 ± 14.1, the number of patients diagnosed with ALF and ACLF was 44.6%, 55.6%, respectively. On admission severity score as follows: SOFA score was 8.2 ± 3.6, MELD score was 26.9 ± 8.1, APACHE II score was 14.0 ± 7.7. DPMAS reduced 25.98% total bilirubin, 27.6% direct bilirubin, reduced inflammatory markers such as NH3, CRP. Mortality rates within 30 days on acute-on-chronic liver failure patients was 46.7%.

Conclusion: DPMAS effectively reduced total bilirubin, direct bilirubin, GOT, GPT.

Acute Renal Failure in Children. Multicenter Prospective Cohort Study in Medium-Complexity Intensive Care Units from The Colombian Southeast

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Background: Acute kidney injury is frequent in critically ill children; however, it varies in causality and epidemiology according to the level of patient care complexity. A multicenter prospective cohort study was conducted in four medium-complexity pediatric intensive care units from the Colombian southeast aimed to estimate the clinical prognosis of patients with diagnosis of acute kidney injury.

Methods: We included children >28 days and <18 years of age, who were admitted with diagnosis of acute kidney injury classified by Kidney Disease Improving Global Outcomes (KDIGO), during the period from January to December 2017. Severe acute kidney

injury was defined as stage 2 and stage 3 classifications. Maximum KDIGO was evaluated during the hospital stay and follow up. Length of hospital stay, use of mechanical ventilation and vasoactive drugs, use of renal replacement therapy, and mortality were assessed until discharge.

Results: Prevalence at admission of acute kidney injury was 5.2% (95%CI 4.3% to 6.2%). It was found that 71% of the patients had their maximum KDIGO on day one; an increment in the maximum stage of acute kidney injury increased the pediatric intensive care unit stay. Patients with maximum KDIGO 3 were associated with greater use of mechanical ventilation (47%), compared with maximum KDIGO 2 (37%) and maximum KDIGO 1 (16%). Eight patients with maximum KDIGO 2 and 14 with maximum KDIGO 3 required renal replacement therapy. Mortality was at 11.8% (95%CI 6.4% to 19.4%).

Conclusion: Acute kidney injury, established and classified according to KDIGO as severe and its maximum stage, was associated with worse clinical outcomes; early therapeutic efforts should focus on preventing the progression to severe stages.

54

Acute Kidney Injury in Newborns in Popayán - Colombia. Multicenter Prospective Cohort Study

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Background: Acute kidney injury (AKI) is a frequent condition in critical newborns, characterized by a decrease in kidney function and associated with poor outcomes. It is considered an important cause of neonatal mortality. A multicenter prospective cohort study was conducted in three neonatal intensive care units of Popayán, Colombia to evaluate the clinical course of AKI and their outcomes.

Methods: Prospective cohort study, we included newborns >2 and <28 days admitted with diagnosis of AKI according to neonatal modified Kidney Disease Improving Global Outcomes (KDIGO), during the period from June 2019 to December 2020. Chromosome incompatible with life, major kidney malformations and severe congenital heart disease were excluded. Perinatal history, comorbidities, and management were assessed. A seven-day follow-up was carried to identify the recuperation of kidney function, need for renal replacement therapy, or death.

Result: We enrolled 21 patients during the period from June to December 2019. The median gestational age was 35 weeks (29 to 39 weeks). 38% had perinatal history of inadequate prenatal control and 28% of gestational infection. The most frequent comorbidities were sepsis in 95% and perinatal asphyxia in 62%. All of the patients were treated with nephrotoxic medications. According to severity, 62% were classified in stage 1, 19% in stage 2, and 19% in stage 3. Stage 1 was more common in preterm and term births. We found more patients stage 3 in term newborns. Con-

cerning the outcomes, 72% recovered their kidney function during the follow-up, 5% needed renal replacement therapy and the mortality was at 14%.

Conclusion: In this outcome of the first six months of the cohort, sepsis, perinatal asphyxia, and high use of nephrotoxic medications were observed. AKI was more frequent in premature newborns but was more severe in term births. In critical newborns, AKI is related to elevated mortality.

55

Comparison of Efficacy Between Maintenance Hemodialysis and Their Combination with Hemoperfusion in Patients Undergoing Chronic Hemodialysis Treatment

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Background and Aims: The occurrence of mid- and long-term uremic complications is related to the low clearance rate of middle and large molecule uremic toxins when haemodialysis (HD) alone is adopted. The objective of this study is to evaluate the efficacy of the combination of maintenance HD with hemoperfusion (HP-HA130) therapy.

Method: A total of 36 patients who underwent routine HD were randomly divided into three groups: Group 1 (n=17): received HD + HP (HA130), (HD 3times/W +HP biweekly). Group 2 (n=10): given HD with high flux dialyzer 3 times a week. Group 3 (n=9): given HD with low flux dialyzer 3 times a week. Before and after the observational period blood samples were taken for haemoglobin (Hb), iron (Fe), total iron binding capacity (TIBC), albumin (Alb), calcium (Ca), phosphorus (PO4) and parathyroid hormone (PTH).

Results: Patients in group 1 had significantly higher values of TIBC (p<0.05) and significant lower levels of PO4 (p<0.01), there was no significant differences of EPO doses and albumin levels between the 3 groups after the follow up period. In the group 1, serum PO4 levels were significantly lower (p<0.05) and TIBC was significantly higher (p<0.05) after the 4 months of the follow up period than it was at the beginning. In group 2 the values of TIBC were significantly lower after the follow up period than it was at the beginning (p<0.05). No statistical difference between groups after the follow up period was observed in terms of Hb, Fe, PTH, Ca, BMI, duration of dialysis treatment and vascular access.

Conclusion: This combination treatment of HD with HP HA130 was superior to HD in reducing levels of phosphorus. These findings suggest a potential role of reducing the risk of cardiovascular events in this population. Also, patients who underwent the combined treatment showed higher values of TIBC, these results eventually demonstrate their role in the improvement of renal disease anaemia, however researches on a larger sample size are needed.

Hemoperfusion in Triple Valve Endocarditis Surgery

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Background: Inflammatory response due to the cascades of blood expose to CPB (Cardiopulmonary Bypass) circuit has been extensively discussed^[1]. The better outcomes of inflammatory modulation by cytokine scavenger in septic patients has been led to the rationale of using hemoperfusion for same purpose during and after cardiopulmonary bypass procedures^[2]. We reported a patient with triple valve endocarditis who underwent cardiac surgery. Hemoperfusion was applied during the CPB operation to reduce intra and postoperative inflammation and complications.

Methods: A 27- years old male was admitted to the cardiac surgery department 10 days before the surgery. Patient was diagnosed with pancarditis, sepsis, significant pericardial effusion, massive bilateral pleural effusions, cardiac cirrhosis, ascites, MOF, AR 4+, MR 4+, TR 4+, severe PHT, NYHA IV. Duration of CPB was 224 min. Combine use CPB and Haemoperfusion (JAFRON HA330) for modulation of the inflammatory response remain for 220 min. Hemodynamic status, inflammatory condition, oxygenation, and other postoperative measurements were observed.

Results: Mitral, tricuspid and aortic valve replacement was completed. The duration of CPB was 224 min and combine duration with HA330 Haemoperfusion was 220 min. The patient was successfully weaned from CPB. Patient was extubated 1 POD, chest tubes were removed on the 1st and 2nd POD. Laboratory findings (CRP, total bilirubin, AST and ALT) show improvement after HP+CPB, x-ray and lung auscultation findings were satisfactory with saturation on room air about SpO₂ 99%. Hemodynamic stability was constant with systemic tension of 105/76 mmHg on low dose of one inotropic drugs and with sinus rhythm and HR 100/min. Repeated transesophageal and transthoracic echocardiography showed improvement in LV ejection fraction without any other pathological findings. Discharged from our Clinic to Clinic for Infective Diseases was on 8th postoperative day for planed long-lasting antimicrobial treatment of endocarditis. Laboratory findings before discharge were within normal limits. The application of hemoperfusion during Cardiac Surgery showed a promising results in decreasing inflammation and improving the outcomes.

Conclusion: Using the cytokine removal devices during the Cardiac Surgery may control the inflammatory response, alleviate the inflammation conditions and improve the hemodynamic status and the overall outcomes.

Therapeutical Approach of HA330 Absorber in Case of Sepsis in Children

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Background: Sepsis is one of the most common causes of hospitalizations and deaths in the world and defined as life-threatening organ dysfunction caused by a dysregulated host response to infections. The final event of this dysregulated and intense inflammatory response is a cytokine storm mainly, which leads to multiple organ dysfunction if it cannot be controlled and stopped by the medical management.

Methods: New therapeutical resources are under investigations in order to further improve the prognosis of the most severe patients affected with sepsis. One of those therapies is the extracorporeal blood purification therapy with hemoabsorbent device HA330 (Jafron Biomedical Co., Ltd, China), which aims to eliminate endo- and exotoxins from the blood during the most severe inflammatory conditions. So far this therapeutical approach was successfully used in a few adult septic patients. Here, we describe and discuss three ALL children who developed severe sepsis and underwent extracorporeal blood purification using HA330 filter.

Results: We applied the HA330 hemoabsorption in a three pediatric patients hospitalized in the PICU and diagnosed with septic shock. The treatment was associated with hemodynamic stabilization and a reduction of procalcitonin, IL6, C-reactive protein. In one case due to "second hit" episode another session with HA330 was run. We also noted that early initiation of therapy leads to faster and more sustainable results.

Conclusion: The treatment with HA330 appeared to be safe and was well tolerated in pediatric patients. The hemodynamic stabilization with reduction of vasopressor needs within hours and reduction of cytokines and inflammation markers were the main conclusions drawn from the use of HA330 in pediatric patients.

Hemoadsorption with HA 230 Adsorber in Case of Acute Delayed Methotrexate Clearance in A Child with Acute Lymphoblastic Leukemia After High-Dose Chemotherapy

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Background: High dose methotrexate (HDMTX) has proven an effect in the treatment of different type malignancies in children, including ALL, non-Hodgkin lymphoma, osteosarcoma and others. However, HDMTX is likely to cause a number of side effects. A number of studies have been published demonstrating the use of extracorporeal detoxification methods for the treatment of MTX delayed clearance (DMC). However, for various reasons, none of the methods is universally safe and effective.

Methods: An eight-year child (weight – 18 kg, S- 0.79m²) was admitted to the "University Medical Center" with the diagnosis of ALL FabL2, T – IV type, high risk group, neuroleukemia. Taking into account clinical and laboratory data, HDMTX (in a dose of 5 grams per m²) was started and plasma-MTX (p-MTX) at the end of the 24 hours MTX-infusion reached 669 µmol/l. conventional treatment during next 12 hours (36 hours after the HDMTX was started) had resulted in no positive change in patient condition and the child has developed acute kidney injury (AKI) in combination with DMC, which was reason to transfer patient in to the intensive care unit (ICU). AKI led to the initiation of pediatric (continuous veno-venous hemodiafiltration) CVVHDF with the "Prismaflex" device (Baxter, US) and the HA-230 adsorber (Jafron, Zhuhai City, China) was initiated and maintained for the next 4 hours.

Results: A single procedure of CVVHDF combined with HA-230 adsorption resulted in reduction of p-MTX from 540.7 to 79.60 µmol/l immediately (reduction rate is -85.27%) during the four hours. The routine blood biochemistry and hematologic parameters improved, as well clinical condition. During the entire procedure, the patient continued to receive the leucovorin rescue protocol.

Conclusion: Management of methotrexate toxicity using the HA-230 adsorber in case of DMC showed 85.27% reduction rate during the single 4 hours procedure and well tolerated in a pediatric patient with ALL.

Does Removal of inflammatory Factors During Bypass Improve Outcome in High-Risk Patient Undergoing Cardiac Surgery?

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Objective: To investigate whether removal of proinflammatory factors during cardiopulmonary bypass (CPB) improves the postoperative outcomes for the high-risk patients undergoing cardiac surgery.

Methods: This prospective, randomized, controlled study included adult patients (over 18 years) scheduled for cardiac or vascular surgery under CPB and their EuroSCORE II > 2 combined with the plasma TNF-α over 8.0 pg/mL. Patients who were pregnant, or had long-term glucocorticoid use, or with immune system diseases, or without informed consent were excluded. The patients were randomly divided into HA380 group and Control group. In the former group, an adsorber (HA380 hemoperfusion cartridge, Jafron Biomedical Co., China) was used continuously during CPB.

The primary outcome were composite events, including all-cause mortality in 30-day, permanent or transient neurological dysfunction, new onset myocardial infarction or low cardiac output, renal failure, acute respiratory disease syndrome, intestinal bleeding or ischemia, and prolonged intubation time (> 24-hours). The secondary outcomes were hospitalization time, blood product consumption and chest drainage.

Results: A total of 40 patients were included into the study (20 in each group). Their demographic characteristics were comparable between groups. There were no significant difference between control group and HA380 group regarding the preoperative complications, EuroScore II, surgical types, CPB time, and cross-clamp time.

The composite events occurred in 4 (20%) patients in HA380 group, and in 7 (35%) patients in control group (p=0.48). Both hospitalization time and blood product consumption were similar between groups, but the chest drainage after 4 hours were slightly lower in HA380 group (median: 75 mL) than that in control group (median: 150 mL) (p=0.19). Although there were no significant differences regarding to peak plasma levels of creatinine, bilirubin, transaminase, troponin between groups (all p>0.1), TNF-α levels (28±12 pg/mL vs. 30±17 pg/mL, p=0.78), counts of leukocyte (median: 7.5*10⁹/L, vs 10.9*10⁹/L, p=0.08), neutrophil (5.9 *10⁹/L vs 8.3*10⁹/L p=0.11) and monocyte (0.36 *10⁹/L vs 0.64 *10⁹/L, p=0.02) were slightly lower in HA380 group than control group.

Conclusion: This prospective, randomized, controlled study showed that removal of inflammatory factors during cardiopulmonary bypass may help to attenuate the systemic inflammation for the high-risk patients undergoing cardiac surgery on CPB. Whether it improves outcomes for these population needs further studies with larger sample size.

Early Use of Endotoxin Absorption by Hemoperfusion Combined With OXIRIS in Septic Shock after Stem Cell Transplantation: A Case Report

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Objective: Endotoxin with secondary release of cytokines can progress to shock and multiple organ failure. We reported an acute lymphoblastic leukemia patient with severe pneumonia and septic shock after stem cell transplantation, which was the case successfully treated with hemoperfusion (HP) combined with continuous renal replacement therapy (CRRT) and a newly designed endotoxin adsorption system oXiris with HP (380).

Method: A 49-year-old woman with acute lymphoblastic leukemia received stem cell transplantation. After 13 days' transplantation her body temperature was still very high and her blood pressure decreased to 72/45 mmHg with oliguria and cardiopulmonary insufficiency, requiring extracorporeal respiratory support and large doses of noradrenaline for resuscitation. Her B-type natriuretic peptide was 32200ng/L, while white blood count was $1.05 \times 10^9/L$, percentage of neutrophils was 81.0%, and plasma procalcitonin (PCT) was 24.70ng/mL, interleukin-6(IL-6) levels above 5000pg/mL. Since blood culture returned positive for Methicillin-resistant coagulase-negative staphylococci and the bacterial culture of sputum subsequently showed growth of Carbapenem-Resistant Pseudomonas aeruginosa, and the patient had severe low blood pressure, hypoxemia and oliguria, combined with the laboratory tests results, he was diagnosed with septic shock, acute kidney injury, and multiple organ failure. It was performed to undergo hemodialysis therapy with hemoperfusion (HA380) combined with CRRT oXiris.

Results: After 12 hours of blood purification therapy with a oXiris filter plus hemoperfusion with a HA380, IL-6 decreased from above 5,000 pg/mL to 116.20 pg/mL and also PCT decreased sharply from 24.70ng/mL to 11.61pg/mL. The duration of blood purification therapy was 66 hours with hemoperfusion (HA380) combined with CRRT oXiris, and hemoperfusion was performed for four times, significant decrease in PCT (3.96ng/mL) and IL-6 (22.28 pg/mL) were observed. Treatment with antibiotics and other drugs were also applied to the patient at the same time. The total sequential organ failure assessment (SOFA) score decreased from 13 to 7. Urine output steadily increased to 250 mL/h, and vital signs and blood pressure were stable without noradrenaline. In the end, her kidney function had completely recovered and she successfully attempted separation from the ventilator.

Conclusion: CRRT (oXiris) combined with hemoperfusion(HA380) which had strong capacity of endotoxin and cyto-

kines adsorption appeared to accelerate improvement in organ dysfunction and ultimate survival in our patient. This could be an important therapeutic method supplement to control infection in critical patients with septic shock after stem cell transplantation for leukemia. Our experience suggests that oXiris CRRT combined with hemoperfusion (HA380) therapy is an effective treatment for septic shock after stem cell transplantation.

Extracorporeal Blood Purification (ECBP) in Critically Ill Septic Patients

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Background: Sepsis is the host response to infection which accompanied with cytokines production or even organ failure. Extracorporeal blood purification therapies are adopted for organ supports especially in intensive care. We are presenting the cases series to evaluate the feasibility and safety of hemoadsorption, efficacy of hemoadsorption in disease's severity improvement and impact on parameters considered to be related with sepsis severity or outcome.

Methods: 6 patients with septic shock and with over 2 organ failures were included. All patients received hemoadsorption (HA) therapy (HA330) once a day as one session for three consecutive days. Modified SOFA score (SOFAM), oxygenation, hemodynamic status and vasoactive drugs requirement and inflammatory parameters were observed for 7 days.

Results: All patients completed HA treatment with improvement of oxygenation. Most of them had PO₂/FiO₂ values ≤ 200 (severe ARDS), with an increase to >250 throughout the monitoring period (even after only the 1st session of HA). Disease severity evaluated using SOFA score decreased due to respiratory and/or cardiovascular benefit. We observed a reduction of the need for vasoactive drugs and improvement of "Cardiac Performance" with amelioration of hemodynamic status. PCR downward-trend after the 1st HA session and PCT decrease were observed in all of the patients. No complications or severe adverse events during the treatment.

Conclusion: Hemoadsorption is simple and compatible with CRRT machines and with good safety. Septic patients appeared to have improved respiratory and cardiovascular performance and hemodynamic parameters' amelioration after HA treatment. Hemoadsorption may benefit critically ill septic patients with significant reduction of sepsis severity. Hemoadsorption may turn out to a therapeutic method to "buy crucial time" within which reversibility is thought to be possible in sepsis.

Blood Purification Therapy with a Hemodiafilter Featuring Enhanced Adsorptive Properties for Cytokine Removal in Critically-Ill Septic Patients

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Background and objective: Sepsis often leads to multiple organ failure, including acute kidney injury (AKI). Renal replacement therapy (RRT) in combination with sequential extracorporeal blood purification therapies (EBP) might support renal

function, attenuate systemic inflammation, prevent or mitigate multiple organ dysfunction in sepsis. The aim of this study is to describe overtime variations of clinical and biochemical features of critically-ill septic patients treated with EBP with a hemodiafilter characterized by enhanced cytokine adsorption properties (oXiris membrane).

Methods: Prospective, multicenter, observational study performed on data recorded into the oXirisNet Registry (aRRT - <http://www.rrt.eu/>), an Italian registry on patients with multiple organ dysfunction who have undergone EBP with the oXiris membrane. We considered data of septic patients admitted to the ICU between May 2019 and April 2020, and who received treatment with oXiris membrane for immunomodulation and/or support to renal function during AKI. Objectives of this preliminary study was to assess the variation of multiorgan dysfunction scores overtime. Clinical evaluations were performed immediately before

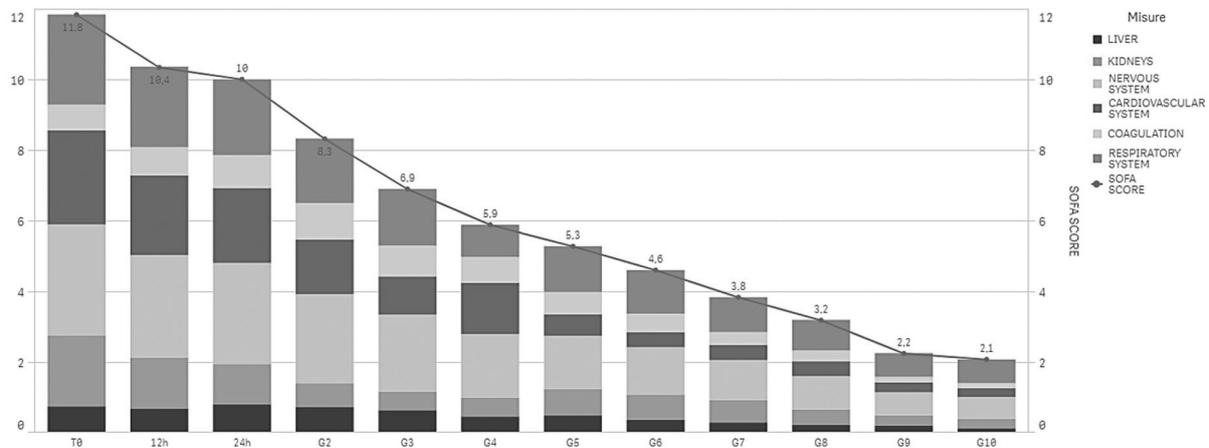


Fig. 1. SOFA score improvement during the observation period.

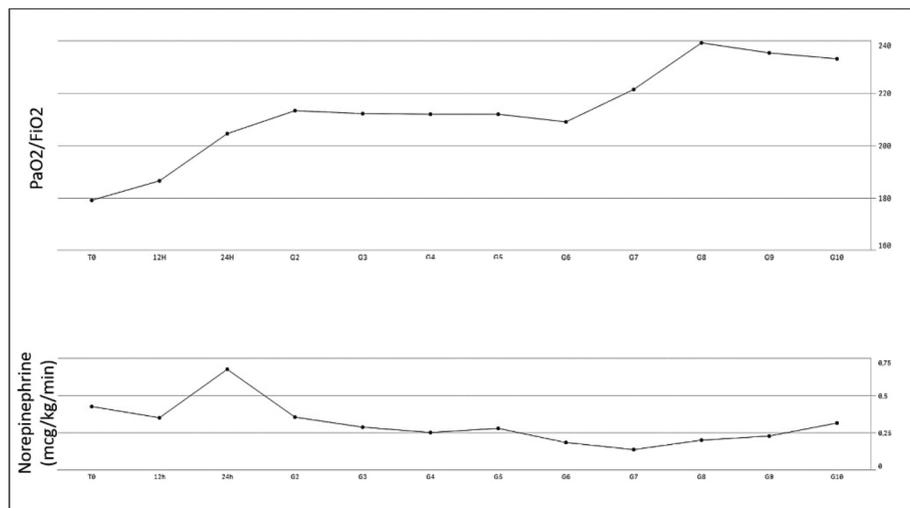


Fig. 2. Horowitz index and Norepinephrine dosage daily variation.

EBP initiation (T0), after 12 hours (T1), and every 24 hours thereafter for the first 10 days from T0. Follow up ended either at ICU discharge or death if it occurred in the ICU.

Results: The study evaluated 68 critically-ill septic patients. Indications for EBP with oXiris in this cohort were: biochemical and clinical evidence of systemic inflammation associated with 1) AKI with absolute indications for RRT or 2) hemodynamic instability and/or multiorgan dysfunction in patients whose renal functional reserve was considered not adequate to sustain metabolic burden of expected fluid overload. AKI was the cause of initiation of EBP in 48 (70.6%) patients; 20 of them presented a KDIGO stage 3, while 28 a KDIGO stage 2. Specific indication of treatment for these patients was: fluid overload in 40 (83.3%) patients, control of uremic solutes in 20 (41.6%), and adjustment of hydroelectrolytic balance in 10 (20.8%) patients. The remaining 20 (29.4%) patients were treated with EBP even in absence of renal indications; all of them were in KDIGO stage 1. EBP treatment duration was 65 hrs (first treatment). 25% of patients underwent a second treatment with oXiris. Median baseline SOFA was 11.8 (IQR 6) and decreased significantly overtime ($p < 0.001$ at Kruskal-Wallis test) during the first 72hrs of the treatment, with most significant decrease in the first 48hrs (median 8.3 IQR 5, $p = 0.001$), and more generally during the 10 days after EBP initiation (Fig 1). The SOFA items that showed most improvement with treatment related to the hemodynamic stability (in terms of vasoactive requirements and norepinephrine dose) and lung functions (quantified in terms of PaO₂/FiO₂ ratio), Fig 2.

Conclusion: The use of the oXiris filter represents a valid option in the management of septic critically ill patients, with or without acute kidney injury. Critically-ill septic patients treated with EBP with heparin-coated hemodiafilter featuring cytokine adsorption properties have experienced attenuation of systemic inflammation and multiorgan dysfunction improvement.

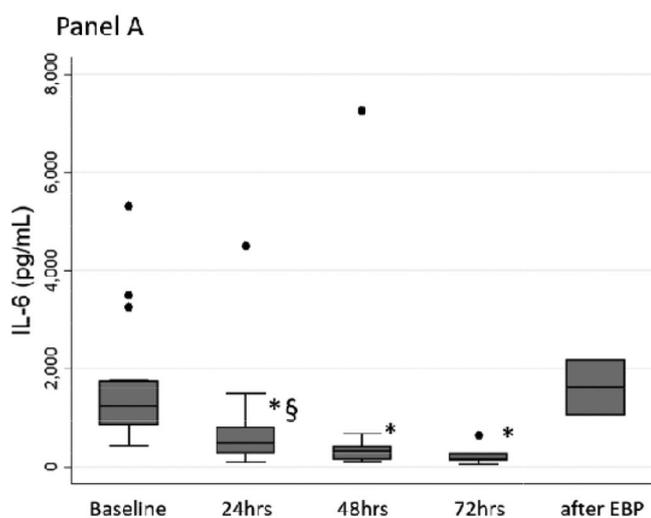


Fig. 1.

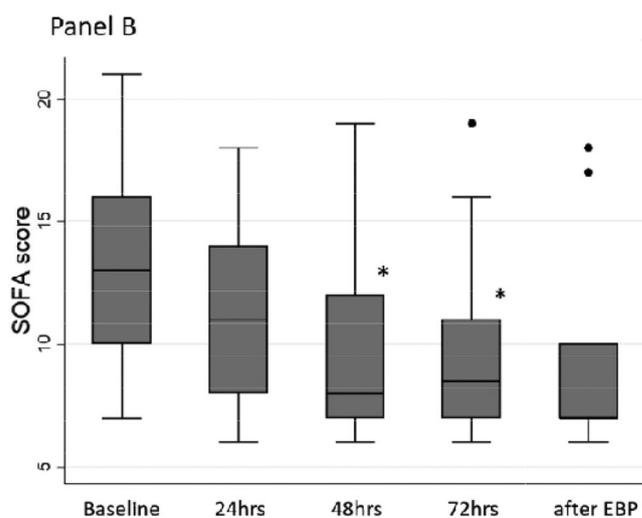
Blood Purification Therapy with a Hemodiafilter Featuring Enhanced Adsorptive Properties for Cytokine Removal in Patients Presenting COVID-19

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Background: Systemic inflammation in COVID-19 often leads to multiple organ failure, including acute kidney injury (AKI). Renal replacement therapy (RRT) in combination with sequential extracorporeal blood purification therapies (EBP) might support renal function, attenuate systemic inflammation, prevent or mitigate multiple organ dysfunction in COVID-19. The aim of this study is to describe overtime variations of clinical and biochemical features of critically-ill patients with COVID-19 treated with EBP with a hemodiafilter characterized by enhanced cytokine adsorption properties (oXiris membrane).

Methods: Prospective, multicenter, observational study performed on data recorded into the oXirisNet Registry (aRRT - <http://www.arrt.eu/>), an Italian registry on patients with multiple organ dysfunction who have undergone EBP with the oXiris membrane. We considered data of septic patients admitted to the ICU between February and April 2020, and who received treatment with oXiris membrane for immunomodulation and/or support to renal function during AKI. Main endpoints included overtime variation of IL-6 and multiorgan function scores, mortality, occurrence of technical complications or adverse events. Clinical evaluations were performed immediately before EBP initiation (T0),



after 12 hours (T1), and every 24 hours thereafter for the first 72 hours from T0. Follow up ended either at ICU discharge or death if it occurred in the ICU.

Results: The study evaluated 37 patients with COVID-19. Median baseline IL-6 was 1230pg/ml (IQR 895) and decreased significantly overtime ($p<0.001$ at Kruskal-Wallis test) during the first 72hrs of the treatment, with most significant decrease in first 24hrs ($p=0.001$), Fig 1. The reduction in serum IL-6 concentrations correlated with improvement in organ function, as measured in decrease of SOFA score ($\rho=0.48$, $p=0.0003$). Median baseline SOFA was 13 (IQR 6) and decreased significantly overtime ($p<0.001$ at Kruskal-Wallis test) during the first 72hrs of the treatment, with most significant decrease in the first 48hrs (median 8 IQR 5, $p=0.001$), Fig 1. Compared to the expected mortality rates, as calculated by APACHE IV, mean observed rates were 12.2% lower following treatment. Best improvement in mortality rate was observed in patients receiving EBP early on during the ICU stay. Premature clotting (running <24 hrs) was observed in patients (18.9% of total) which featured higher effluent dose (median 33.6ml/kg/hr, IQR 9) and higher filtration fraction (median 31%, IQR 7.4). No electrolyte disorders, catheter displacement, circuit disconnection, unexpected bleeding, air- or thromboembolisms due to venous cannulation of EBP were recorded during the treatment. In one case infection of vascular access occurred during RRT, which required replacement.

Conclusion: In patients with COVID-19, EBP with heparin-coated hemodiafilter featuring cytokine adsorption properties was performed without adverse events. During the treatment, patients have experienced serum IL-6 levels reduction, attenuation of systemic inflammation, multiorgan dysfunction improvement and reduction in expected ICU mortality rate.

64

Six-Year CRRT Experience in a Single Center PICU: A Retrospective Cohort Study

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Background: In-hospital acute kidney injury (AKI) is common among critically-ill children and young adults. AKI in the Pediatric Intensive Care Unit (PICU) setting is associated with prolonged hospital stay and poor outcome, especially when Continuous Renal Replacement Therapy (CRRT) is needed. The aim of this study is to describe clinical characteristics, biochemical features, and outcomes of critically-ill children treated with CRRT in our pediatric center, and to analyze factors that can affect the success of a single CRRT session.

Methods: This is a six-year retrospective, single center, observational study including all consecutive patients aged 0 to 18 years who received CRRT during PICU stay at the Meyer Children's Hospital from January 2012 to December 2017. Collected data included main anthropometric, physiologic and biochemical parameters, comorbidities and disease-associated symptoms. Clinical

and technical evaluations were performed immediately before CRRT initiation (T0), at CRRT discontinuation, and per each CRRT session. The last available follow-up after PICU discharge was considered as long-term outcome.

Results: One-hundred and one CRRT session were performed on 23 patients. The mean age and weight were 1.9 years and 19.5 Kg. CRRT was started on average after 3.5 days from PICU admission, mostly for severe AKI (59%). Continuous veno-venous Hemodiafiltration (CVVHDF) was preferred in 82.6% of cases and systemic heparinization was the most applied anticoagulation method (69.6%). Fifty-three from PICU admission treatments were interrupted for clotting (average treatment duration was 50.5 hrs), while 48 treatments were interrupted for clinical decision (mean treatment duration was 67.1). Among treatment-related parameters higher post-replacement fluid flow correlated with an increased risk of clotting $p=0.0422$, while clotted and not-clotted treatments had similar Net UF set overtime. Hemodynamic instability requiring vasopressors was observed in 43.5% of cases. Mortality rate was 39.1%, with only 14/23 patients successfully discharged from the PICU. Among the 14 patients discharged from the PICU, two were lost to follow-up soon after discharge and four died from complications of their primary disease (two of them showing Chronic Kidney Disease (CKD) at last follow-up). Among the remaining eight patients, three were not addressed to nephrology follow-up, while five are currently attending regular work-up in the Nephrology Unit. In total, CKD developed in 41.6% of PICU survivors, with a median follow up of 2.5 years.

Conclusion: CVVHDF with heparin anticoagulation was the most common prescription adopted in this cohort of consecutive pediatric critically-ill patients requiring CRRT. Clotting was a frequent complication and it was particularly associated with prescription of higher convective dose. Long-term CKD developed in almost half of patients who survived at PICU discharge.

65

Combined Extracorporeal Blood Purification in a Patient with Severe COVID-19 and Septic Shock

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Background: The effective lowering of proinflammatory cytokines' concentration by cytokine sorption (CS) and selective plasma exchange (SPE) was demonstrated in sepsis¹. Taking into account the different mechanism of cytokine hyperproduction in COVID-19 compared to sepsis, EBP may have additional benefits and even improve outcomes. A combination of CS and SPE in patients with severe COVID-19 may be more effective than each method when used separately. Our experience of successful treating severe COVID-19 with cytokine storm, complicated by sepsis and septic shock is demonstrated in this case.

Method/Case Presentation: A 69-year-old lady admitted with COVID-19 and deteriorated on day 3 of hospital stay. Cytokine storm with respiratory and circulatory failure was diagnosed with CRP level of 298 mg/l and COVID-19 pneumonia with 90% lung

tissue involvement on CT. She was transferred to an ICU where NIV, infusion therapy and tocilizumab were started. After 2 days she was intubated because of the respiratory failure progression and cerebral dysfunction. Septic shock was diagnosed soon with PCT level of 2.2 ng/ml, hypercytokinemia with IL-6 of 2491 pg/ml, ferritin of 4642 mcg/l and acute renal, liver and circulatory failure. SPE with Evaclio 2C20 was followed by three consecutive CS's with two Jafron HA330 cartridges attached simultaneously during the first procedure and one cartridge for the each next session. There were circulatory, renal and liver failure resolution, complete weaning from vasopressors after the first CS procedure. She was switched to spontaneous breathing in 2 days after the last CS and decrease of IL-6 level to 161 pg/ml, ferritin of 35 mcg/l, PCT of 0,24 ng/ml was seen. She was rehabilitated and discharged on day 39 of hospital stay.

Conclusion: CS in combination with SPE can be effective in treating patients with severe COVID-19, complicated by bacterial co-infection with sepsis and septic shock.

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66

Report on Case Series of Acetaminophen Poisoning at Cho Ray Hospital. Reviewing the Role of Hemoperfusion in Treatment of Acute Poisoning

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Abstract: Nowadays, most cases of drug or chemical poisoning are treated primarily by intensive medical care. Intensive supportive measures such as hemodialysis or hemoperfusion may be helpful in patients with severe complications who need removing toxic agents. The factors influencing to the removal of toxins by hemodialysis and hemoperfusion are understood partly clearly. As a practical guide, drugs that can be eliminated with both techniques will be presented and updated periodically according to the development of techniques of producing filtration membrane.

Although nephrologists and emergency and critical care physician usually deal with dialysis-related decisions in treatment for poisoning case because of their popularity, although, the mortality rate is not high. The role of hemodialysis and hemoperfusion in the treatment for poisoning is frequently discussed in the field of Resuscitation and Poison Control when mention to techniques used to treat poisoning patients such as hemofiltration, continuous dialysis (CAVH, CVVH), plasma plasmapheresis (PP) and blood transfusion. Chelation agents may require a combination of hemo-

dialysis and hemoperfusion (HD and HP), for example, aluminum, iron, thallium, mercury and other metal poisoning cases)².

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67

Cytokine Removal Therapy in Sepsis—Case Report

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Case presentation: A 79 years-old male admitted to the ICU from the OR after emergent surgery due to suture dehiscence and diagnosed of fecaloid peritonitis and septic shock with MODS. He was hemodynamically unstable, with unresponsiveness to fluids and received high doses of vasopressors (up to 1.7 µg/kg/min of noradrenaline), peripheral hypoperfusion, increase in lactate (3.5 mmol/L) and low urine output.

Lab tests showed lactic acidosis, low white blood cell ($2.59 \times 10^3 / \mu\text{L}$ with neutrophil 62.6%). PaO₂/FiO₂ 158 mmHg. The C-reactive protein (CRP) level was 495.13 mg/L (nv < 10 mg/L), procalcitonin levels were high (5.25 ng/ml, nv < 0.5 ng/ml) IL-6 > 5000 pg/mL (nv < 40 pg/mL). SOFA score 11 points. SAPS III 88 points (predicted mortality 83%). He received meropenem (continuous perfusion) and linezolid. CVVHDF (Baxter Prismaflex) with RCA and three times Hemoperfusion (Jafron HA380) were conducted. Changes of inflammatory mediators, blood pressure, doses of vasopressor, diuresis were monitored. Favorable clinical progression. No major complications related to HP. On day 4 of admission RRT was stopped, on day 5 he was weaned from mechanical ventilation and on day 8 he was transferred to Surgery ward.

Conclusions:

- Cytokine removal therapy should be considered in unresponsiveness septic shock.
- Potential role of HP (isolated or associated with CRRT) for:
 - Decrease cytokines and inflammatory mediators.
 - Stabilize hemodynamic with decrease in requirements for vasopressors.
- Hemoperfusion (HA380) is compatible to CRRT machine (Prismaflex) with optimal safety.
- Safe technique with close and correct monitoring.
- Further clinical study with large samples is expected.