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Selected Abstracts from the

35th Vicenza Course on AKI & CRRT

Vicenza, June 13–16, 2017

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Prevalence and Characteristics of Intradialytic Hypotension – A Two-Months, Prospective Study of 884 Haemodialysis Sessions

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Background: Intradialytic hypotension (IDH) is a very serious clinical problem. It is one of the most frequent complications in renal replacement therapy which diminishes patient's quality of life, and increases mortality in the dialyzed population. There is limited studies investigating its exact prevalence and more over, several definitions of IDH are used. The goal of this study was, to assess the prevalence of IDH, primarily in reference to the European Best Practice Guideline (EBPG) on haemodynamic instability: A decrease in systolic blood pressure (SBP) ≥ 20 mm Hg or in mean arterial pressure (MAP) ≥ 10 mm Hg associated with a clinical event and the need for nursing intervention.

Methods: During 2 months we prospectively collected haemodynamic data, clinical events, and nursing interventions of 884 haemodialysis sessions from 45 prevalent patients who dialyzed with constant dialysate conductivity. Patients were considered as having frequent IDH if it occurred in $>20\%$ of dialysis sessions.

Results: Decreases in SBP ≥ 20 mm Hg or MAP ≥ 10 mm Hg occurred in 35.5%, clinical symptoms occurred in 20%, and nursing interventions were performed in 9.6% of dialysis sessions. Dialysis hypotension according to the full EBPG definition occurred in only 15% of dialysis sessions. Ten percent of patients had frequent IDH. Increased IDH frequency was associated with age, female gender, diabetes, longer end stage renal disease vintage, higher ultrafiltration volume, cardiovascular disease, lower pre-HD systolic blood pressure, Weight gain, higher difference between prescribed and achieved post-HD weight.

Conclusions: IDH frequency was highly variable, associated with individual facilities, patient and treatment characteristics.. Identifying practice patterns associated with IH coupled with routine reporting of IDH will facilitate medical management and may result in the prevention of IDH, decreased mortality, and decreased hospitalization.

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Furosemide-Induced Severe Hypokaliemia with Rhabdomyolysis and AKI in a Patient with Nephrotic Syndrome

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Purpose: A case of severe hypokaliemia and rhabdomyolysis in a patient treated with furosemide is described. Hypokalemia induced by diuretic abuse is a life-threatening emergency.

Summary: A 17-year-old Moroccan boy weighing 55 kg was admitted to the hospital after complaining of facial puffiness and pedal edema for 2 weeks and from myalgias, vomiting and diarrhea for 5 days. His medical history revealed a diagnosis of nephrotic syndrome secondary to minimal change disease when he was 15 years old. He had 1 relapses, the last of which occurred 2 years ago. He had been taking 1 g of furosemide per day for 2 years and had not taken prednisolone for the past 15 days. His vital signs were normal on admission, but anasarca and severe muscle weakness and pain was noticed during general examination. Cardiovascular, respiratory, and abdominal examinations were normal. Relapse of nephrotic syndrome was considered, and his 24-hour urine protein value confirmed the diagnosis. Blood tests revealed hypokalemia with a lowest value of 1.6 mmol/l, moderate hyponatremia, metabolic alkalosis, acute kidney injury and important creatinophosphokinase-elevation. Serum cortisol was normal. Daily boluses of solumedrol were given for 3 days in a row then prednisolone 60 mg p.o. once daily was initiated and spironolactone was initiated. After electrolyte substitution and IV hydration, laboratory abnormalities regressed, muscle weakness was improving slowly and eadema regressed. Follow-up three weeks later revealed a normal CK level and no myopathy-related complaints.

Conclusion: Rhabdomyolysis was reported in a patient with nephrotic syndrome who was treated with high doses of Furosemide. Abrupt withdrawal of prednisolone and the patient's underlying renal impairment may have predisposed the patient to this adverse reaction.

Relation of Positive Fluid Balance to the Severity of Renal Impairment and Recovery Among ST Elevation Myocardial Infarction Complicated by Cardiogenic Shock

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Purpose: Limited data is present regarding the relation of positive fluid balance and acute kidney injury (AKI). We analysed the relationship between a positive fluid balance and its persistence over time on AKI development, severity and resolution among ST elevation myocardial infarction (STEMI) patients complicated by cardiogenic shock.

Methods: We retrospectively studied the cumulative fluid balance intake and output at 96 hours following hospital admission in 84 consecutive adult patients with STEMI complicated by cardiogenic shock, all undergoing primary angioplasty. The cohort was stratified into two groups, based on the presence or absence of positive fluid balance on day 4. Patients' records were assessed for the development of AKI, AKI severity and recovery.

Results: Positive fluid balance was present in 44/84 patients (52%), and 51/84 (60%) developed AKI. Patients having positive fluid balance were more likely to develop a more severe AKI stage (52% vs. 13%; $P < 0.001$) and were less likely to have recovery of their renal function (29% vs. 75%, $p = 0.001$). Patients having positive fluid balance demonstrated positive correlation between the amount of fluid accumulated and the rise in serum creatinine ($R = 0.42$, $p = 0.004$). In a multivariate logistic regression model for the 51 patients with AKI, for every 1 liter increase in positive fluid balance, the adjusted possibility for recovery of renal function decreased by 21% (OR = 0.796, 95% CI 0.67–0.93; $P = 0.006$).

Conclusions: A positive fluid balance was strongly associated with higher stage AKI and lower rate of AKI recovery in STEMI complicated by cardiogenic shock.

Assesment and Management of Hypertension in Patients on Chronic Hemodialysis

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Introduction: Hypertension in subjects on long term dialysis is frequent. Its origins are found in extracellular volume overload. The interaction between these factors may explain why the control of hypertension in dialysis patients requires ongoing attention to the many aspects of good dialysis.

Patients and Methods: We realized a cross sectional descriptive study about 51 hemodialysis patients between October 2016

and January 2017. We determinate two groups of patients: one with high blood pressure and the second without.

Results: The mean age of your patients was 46 years with a female predominance.

The mean duration of hemodialysis was 9.8 years. The initial nephropathy was hypertensive in 9 cases. Of these 41 patients undergoing hemodialysis, 25 were hypertensive when hemodialysis started and 23 required antihypertensive treatment.

15 patients used at least one antihypertensive treatment, in 55.3% calcic inhibitor.

The mean blood pressure before hemodialysis was 154/88 mm Hg. The mean blood pressure duration during hemodialysis was 145/81 mm Hg, and 141/79 mm Hg after hemodialysis.

44% of hypertensive patients had left ventricular hypertrophy and 6.2% had presented an ischemic cardiopathy and 67% non hypertensive patients had a normal cardiac ecoghrapy.

Lipid profile was disrupted 59.7% in cases: 67% of hypercholesterolemia in hypertensive patients.

Conclusion: Hypertension is a major risk factor for cardiac disease. The extra-cellular volume expansion is the main pathophysiological determinant of hypertension in hemodialysis patients. Avoiding hypertension remains a capital goal of maintenance dialysis.

Involvement of Religious Factors on the Attitude Toward Organs Donation Among University Students in Morocco

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Introduction: The attitude toward cadaveric organ donation is modulated by different factors, such as religious beliefs. This study sought to analyze the attitude of University student in Morocco regarding deceased organ donation depending on their religious beliefs.

Material and Methods: A sample of university students of Marrakech ($n = 503$) stratified by age and sex was selected. Data of this cross sectional study was collected by self administered and anonymous questionnaire from 4 universities in Marrakech. The c2 test, Student t test, and logistic regression analysis were used to analyze data.

Results: Of the 503 survey respondents, 40.3% were females, 40.3% were males. 99.4% ($n = 500$) were Muslims, 0.6% ($n = 3$) were Catholic. Mean age of the sample was 21.5 ± 1.7 . 100% of students answered the questionnaire. Majority of students (86.4%) were aware of organ donation in Morocco with media as the main source of information. 57.6% agreed to donate their organs. In the students' opinion, The most commonly donated organs and tissues were kidney and heart. 24.5% of the students thought that organ donation was performed only in Public hospitals. 33.4% were aware of organs that could be transplanted. A significant association between the religious beliefs and attitude toward organ donation among those tested can be objectified: 60.6% of respondents believed their religion was favorable toward donation and

39.4% consider their religion contrary to donation. Among the respondents who considered their religion contrary to donation, only 45.45% were in favor of cadaveric organ donation ($P < 0.001$).

Conclusions: The attitude toward cadaveric organ donation among University students in Morocco are influenced by religious beliefs and consider what their religion says regarding organ donation.

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Heavy Acute Tubular Necrosis Resulting in CKD Stage III as a Consequence of Dapagliflozin Use

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A 50-year old man with type II diabetes, hypertension and dyslipidemia, presented with non-oliguric acute kidney injury (AKI). Renal biopsy showed acute tubular necrosis (ATN) with extensive cytoplasmic vacuolization and areas of tubulitis. These findings were ultimately attributed to dapagliflozin, which he started 3 months earlier due to poor glycemic control. ATN with similar microscopic findings has been described with larger doses of dapagliflozin in non-clinical trials. Our patient was started on dialysis and remained dialysis-dependent for 4 weeks while his renal function improved gradually thereafter. Sixteen months after initial presentation he is being followed as an outpatient with chronic kidney disease (CKD) stage 3a. Dapagliflozin belongs to a novel class of antidiabetic drugs for which clinical trials show great beneficial effects on cardiovascular outcomes and glycemic control and as with many new drugs, their safety profile is being constantly revised. AKI is considered one of the serious side effects of SGLT-2 inhibitors and putative mechanisms include glucosuria-driven osmotic diuresis along with toxicity from altered fructose and uric acid metabolism in the renal tubules. We report the first biopsy-proven ATN caused by dapagliflozin. Great caution together with continuous monitoring of renal function is advised when implementing SGLT-2 inhibitors in clinical practice.

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Extended Outcomes Following Implementation of Transition Care Program for Acute Kidney Injury with Prolonged Dialysis Support

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Introduction: Patients with acute kidney injury (AKI) may need prolonged dialysis support (PDS) beyond index hospitalization. We hypothesize that implementing an AKI transition care program (ATCP) may improve one-year patient outcomes.

Methods: Patients with AKI-PDS, from Sep'12 to Dec'15, were retrospectively studied. Patients under the ATCP (multidisciplinary care to facilitate dialysis support and weaning with in-to out-patient continuum, from Jul'14 onwards) were compared against historical controls. We examined patient mortality and cumulative hospitalization days over one year, and dialysis and catheter days over first 90 days. Outcome-days were expressed as incidence density per 1000 patient-days.

Results: We studied 89 patients (age 62(±15) years, 60% males), 47% having septic AKI, 20% cardiorenal syndrome, 47% diabetes mellitus, 61% and 29% with baseline eGFR <60 and <30 ml/min/1.73 m² respectively. Comparing 45 ATCP patients versus 44 controls: 64% versus 45% received continuous renal replacement therapy (CRRT) ($p = 0.07$), with comparable incidences of heart failure (24% versus 25%), ICU care (67% versus 70%), dialysis successfully weaned (71% versus 75%), respectively. Corresponding (ATCP versus controls) one-year mortality was 24% versus 32% ($p = 0.44$), hospitalization days 205 (197–213) versus 223 (215–232) ($p = 0.002$), with comparable dialysis and catheter days. On multivariate analysis, heart failure or having received CRRT independently predicted one-year mortality ($p < 0.05$) and longer hospitalization days ($p < 0.001$), while ATCP was independently associated with reduced hospitalization days ($p < 0.001$). 17 ATCP patients and 14 controls required outpatient dialysis weaning, with hospitalization days of 121 (112–130) versus 138 (127–148) ($p = 0.02$), and catheter days 607 (568–648) versus 683 (638–731) ($p = 0.01$), respectively.

Conclusions: Implementing ATCP in patients with AKI-PDS was associated with reduced hospitalization days and comparable survival over one year, and reduced catheter days in patients discharged for outpatient dialysis weaning.

Early CRRT Filter Clotting Caused by Hypertriglyceridemia Requiring Therapeutic Plasma Exchange

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Introduction: Early filter clotting of the continuous renal replacement (CRRT) circuit leads to insufficient renal replacement dose and increased costs. Usual causes for early clotting are insufficient circuit anticoagulation and venous access problems. A rare cause for shortened filter life has been described in the literature as hypertriglyceridemia with a handful of parenteral nutrition related cases reported that showed early CRRT filter clotting and reduced filter lifespan. Treatment required discontinuation of the lipid component of parenteral nutrition.

Case Presentation: We present the case of a 67-year-old male patient with a history of hypertension, unidentified familial hyperlipidemia and acute pancreatitis admitted to our department with acute necrotizing pancreatitis due to diet related hypertriglyceridemia. Initial hypertriglyceridemia was treated with therapeutic plasma exchange (TPE) and although triglyceride levels decreased significantly (from 7,699 to 1,230 mg/dL) effectively curbing further pancreatic damage, the patient developed systemic inflammatory response syndrome with cardiovascular instability and KDIGO stage III kidney injury. Continuous venovenous hemodiafiltration was started with regional citrate anticoagulation, but despite adequate anticoagulation parameters, patency of the circuit was severely reduced requiring several unplanned circuit changes. Since potential technical causes were ruled out, ongoing hypertriglyceridemia was believed to be the main contributing factor, which was further proven by the clotted filters showing macroscopic signs of lipid deposits.

TPE was restarted with successful reduction of the serum triglyceride levels to 551 mg/dL. Renal replacement was reinitiated with significantly improved filter lifespans (from 10.7 ± 1.66 to 83 ± 7.1 h; $p < 0.05$, two-tailed T test), delivered dose (from 15.4 ± 2.6 to 35 ± 2.6 ml/kg/h; $p < 0.05$) and decreased costs (from 826 $\pm$ 133 to 430 $\pm$ 24 €/day; $p < 0.05$). TPE was repeated between circuit changes with a more restrictive goal of keeping serum triglyceride levels below 600 mg/dL as opposed to acute pancreatitis treatment goals of 1000 mg/dL.

Discussion: Elevated triglyceride leads to a procoagulant state resulting in disorganized fibrin formation around hemofilter fibres. Previous case reports suggested that efforts to reduce triglyceride levels (modifying parenteral nutrition, avoiding lipid emulsions) improved filter survival, but the exact serum triglyceride treatment goal has not been defined.

Conclusion: Severe cases of acute pancreatitis caused by hypertriglyceridemia often require a complex treatment plan including therapeutic plasma exchange and renal replacement therapy. We suggest considering to adapt a more restrictive goal of triglyceride levels less than 600 mg/dL in cases where continuous renal replacement therapy is initiated in order to ensure adequate filter patency.

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Efficiency of On-Line Haemodiafiltration (HDFOL) Treatment with Polyester Polymer Alloy (PEPA) Dialysis Membrane in Plasma Free Light Chain (sFLC) Removal in Patients with Multiple Myeloma (MM)

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Introduction: Renal failure is a frequent complication in patients with multiple myeloma that causes significant morbidity and mortality. Combination treatment with chemotherapy and dialysis with high-performance filters can be effective in reducing sFLC levels and recovering sufficient renal function and complications in this disease. There is manifold literature on the use of special filters with high cut-off as well as adsorbent filters for removal light chains.

We reported our experience with two patients with light chain disease (IgG-k and IgG- λ respectively) who were treated with HD-Fol using polyester polymer alloy (PEPA) membrane.

Materials and Methods: All treatments in both patients were performed with the following methods: length of dialysis (Td) = 210 min; blood flow (Qb) = 250 ml/min; dialysate flow; (Qd) = 500 ml/min, infusion rate (Qinf) = 50 ml/min in post-dilution mode, filter FDX210GW (PEPA)-NIKKISO®.

During study sessions, at the dialysis start we measured membrane sieving coefficient (SC) for β 2-microglobulin (β 2-M), sFLC-k and sFLC- λ ; free light chains were also measured before and after each session in order to calculate the reduction rate (RR%).

The contribution of diffusion, convection and adsorption to sFLC-k, sFLC- λ elimination by HDFol was investigated through the mass balance calculation.

Table 1. (for Abstract no 9)

Case 1 sFLC-k (n°6 session checked)		Case 2 sFLC- λ (n°3 session checked)	
M _{TR} mg/min	389 $\pm$ 396	M _{TR} mg/min	44.4 $\pm$ 17.7
M _{UF} mg/min	161 $\pm$ 149	M _{UF} mg/min	6.6 $\pm$ 2.8
M _{AD} mg/min	228 $\pm$ 247	M _{AD} mg/min	37.8 $\pm$ 14.8

Fig. 1. (for Abstract no 9).

Results and Conclusion: The overall mean SC were: 0.55 ± 0.02 for sFLC-k, 0.16 ± 0.01 for sFLC-λ and 0.88 ± 0.01 for β2-M. The overall mean RR% were 65.9 ± 4.3 for sFLC-K and 49.5 ± 7.7 for sFLC-λ (Fig. 1).

The total mass removal rate (M_{TR} mg/min) and the comparison of the mass removal rate by ultrafiltration (M_{UF} mg/min) and by adsorption (M_{AD} mg/min) are shown in Table 1.

Our data show a good reduction of sFLC by PEPA filters used in haemodiafiltration comparable to that obtained by filters a higher cut-off (as Theralite).

The removal was due mainly to membrane adsorption: $M_{AD} = 52.5 \pm 5.3\%$ for sFLC-k and $86.3 \pm 1.4\%$ for sFLC-λ.

This dialysis technique may be an effective method at low cost in the light chain disease therapy.

Indications and Outcomes of Plasma Exchange (PE): Five Years of Experience in Critical Nephrology Service in Fundacion Cardioinfantil Bogotá – Colombia

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Introduction: We describe our retrospective data of five years of outcomes and indications for PE in a center in Bogotá – Colombia between 2010 to 2016 we used AquariusTM technology and since then we use PrismaflexTM. We choose albumin or fresh frozen plasma as replacement fluid according to recommendations of ASFA guidelines [1] and according to levels of plasma fibrinogen.

We perform therapy until recovery of the pathology defined with the treating interdisciplinary team.

Results: Between 2011 and 2016 we performed 1466 plasma exchange therapies to 232 patients, 41% were women, mid age of population was 46.6 y.o. PE was performed with albumin in 48% of cases. The mean number of sessions of PE was 6.3/patient (minimal 1–maximal 21).

Previous at the beginning of the PE, all patients were discussed according to the diagnosis of each patient. Indications for all PE were related to ASFA (American Society for Apheresis) since 2010 and according to actualizations on 2013 and 2016¹.

The most frequent indication for PE was derived of the neurological pathologies (29%), predominantly Guillain-Barre syndrome, the second in frequency was Myeloma cast nephropathy (16%) followed by acute graft rejection of heart or kidney transplantation (12%). The therapy was discontinued according to ASFA recommendations or in particular cases later or sooner with a previous interdisciplinary medical joint. The diagnostic of the patient that received 21 sessions was a recurrent FSGS in kidney transplant.

Recovery: most of the patients had recovery of the underlying condition (74%). Guillain Barré and miastenia cases had 100% of recovery. There was recovery in all cases of acute rejection of heart and kidney grafts. We found improvement of kidney function and cessation of dialysis need in 80% of cast myeloma kidney disease.

Mortality was related always with the underlying pathology (18 patients), and never was related with complications of the therapy.

Conclusions: It is remarkable for us that plasma exchange as an extracorporeal therapy requires vast interaction between nephrologists and other specialties, especially in low grade of recommendation therapeutical indication.

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Four Cases of Posterior Reversible Encephalopathy Syndrome (PRES) with Acute and Chronic Kidney Disease. Should We Nephrologists Consider It More Frequently?

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Introduction: Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological condition with manifestations such as headaches, altered mental status, seizures, and visual disturbances that show reversible cortico subcortical vasogenic oedema in Neuroimaging, predominantly involving bilateral parieto-occipital regions.

PRES is associated with clinical factors like blood pressure (BP) fluctuations, acute or chronic kidney disease (AKI/CKD), infection, immunosuppression, autoimmune disease, posttransplantation, cytotoxic drugs and preeclampsia-eclampsia.

The disorder is usually reversible when the cause that precipitates it is treated or eliminated.

PRES is recurrent in patients with uncontrolled hypertension. (5–10%).

Magnetic resonance (MRI) with fluid-attenuated inversion recovery (FLAIR) imaging is gold standard to diagnose and detect subcortical and cortical lesions in PRES.

The following are four patients that suffered from PRES in our hospital in the past 8 years:

Case 1: Female patient, 33 years old with history of arterial hypertension of 1 year of evolution, without adherence to treatment. She was admitted to ICU (intensive care unit) because of hypertensive acute lung edema, oliguria and renal failure. Renal replacement therapy (RRT) was initiated, in different modalities, according to their clinical status, while was on mechanical ventilation.

The patient developed multiple complications such as hypovolemic shock, retroperitoneal hematoma which led to left radical nephrectomy. Then she presented PRES with blindness and altered mental status.

Brain CT showed focal regions of edema in both occipital lobes. MRI showed regions T2 and FLAIR hyperintense signals from subcortical white matter of the occipital lobes.

BP was lowered using antihypertensive agents and continued with RRT. Her symptoms improved and the patient was discharged on regular iHD.

She is currently transplanted.

Case 2: Female patient, 29 years old, history of arterial hypertension with CKD with peritoneal dialysis treatment. She was admitted to ICU because of altered mental status, seizures and hypertension.

Her symptoms and hypertension worsened after being admitted and she began experiencing blindness and multiple generalized tonic-clonic seizures that lasted several minutes and eventually progressed to coma. She required mechanical ventilation and was treated with antihypertensive and antiepileptic drugs.

Her neurological symptoms and general condition improved the fifth day of treatment.

Table 1. Summary of the patient's history, MRI findings and final outcome (for Abstract no 11)

	Case 1	Case 2	Case 3	Case 4
Year	2009	2013	2014	2016
Gender	Female	Female	Female	Female
Age (years)	33	29	71	20
Primary renal disease	Unknown	Unknown	Hypertension	SLE
Transplantation	No	No	Yes	No
Trigger	Hypertension Abdominal infection	Hypertension	Hypertension Cyclosporine Respiratory infection	Hypertension/ LES with no treatment
Clinical findings	Hypertension, blindness, altered mental status	Hypertension, seizure, blindness, altered mental status	Hypertension, altered mental status	Hypertension, seizure, altered mental status
Renal treatment	CHDF, CHD, plasmapheresis and iHD	Peritoneal Dialysis	No	eHD, iHD, Plasmapheresis
Recurrency	No	No	No	Yes
Lesions on CT	Bilateral occipital lobes	No lesion	No lesion	No lesion
Lesions on MRI	Didn't have MRI done	Thalamic, protuberancial and Bilateral parieto occipital lobes	Bilateral occipital lobes	Bilateral parieto occipital lobes
Outcome	Resolution/ Transplantation	Resolution/ transplantation	Resolution	Resolution/ HD

CHDF, continuous haemodiafiltration; CHD, continuous haemodialysis; CT, computed tomography; Ehd, extended haemodialysis; iHD, intermittent haemodialysis; MRI, magnetic resonance imaging; LES, systemic lupus erythematosus; RRT, renal replacement therapy.

BP was lowered and the patient could continue with peritoneal dialysis.

EEG (electroencephalogram) was normal.

Brain CT showed no lesion.

Brain MRI showed regions T2 and FLAIR hyperintense signals at thalamic, protuberancial regions and subcortical white matter of the bilateral parieto occipital lobes.

DWI (diffusion) was negative.

The patient was discharged and continued regular peritoneal dialysis.

She is currently transplanted.

Case 3: Female patient, 71 years old with history of chronic obstructive lung disease, arterial hypertension, CKD and renal transplantation, receiving treatment with cyclosporine and prednisone. She was admitted to the ICU due to acute lung injury, elevated BP and acute renal failure.

She required mechanical ventilation and antibiotic therapy that was initiated empirically considering an initial diagnosis of pneumonia.

She became afebrile with improvement of the symptoms and was successfully extubated.

Hypertension eventually worsened, and patient evolved with visual disturbances and altered mental status.

Brain CT showed hyperintensity in both occipital lobes, MRI showed regions T2 and FLAIR hyperintense signals in those same regions.

BP was lowered using antihypertensive agents and her symptoms improved.

She was discharged and 1 month later her control MRI was normal.

Case 4: Female patient, 20 years old, history of a 2 month old nephrotic syndrome. She was admitted to ICU because of oliguria, renal failure and high blood pressure, that required starting treatment with antihypertensive drugs. Because of persistence of oliguria, RRT was initiated using different modalities according clinical status.

Blood testing and renal biopsy diagnosed SLE (Systemic lupus erythematosus), so patient started treatment with plasmapheresis, steroids and cyclophosphamide.

During her stay in ICU, she suffered seizures in the context of hypertension and progressed to coma. Symptoms that improved with control of the blood pressure and 6 sessions of plasmapheresis.

Brain CT showed no lesion.

Brain MRI showed regions T2 and FLAIR hyperintense signals at thalamic, and protuberancial regions and subcortical white matter of both parieto occipital lobes.

DWI was negative.

EEG was normal.

She suffered two other seizures in the context of high levels of blood pressure.

Her neurological symptoms and general condition improved and the patient was discharged on regular iHD.

Discussion: The syndrome of posterior reversible encephalopathy (PRES) is a rare disease related to different clinical entities and different pathophysiological origins, not yet clarified with different theories to explain it. This condition causes a delay in diagnosis.

Our presentation shows examples of the same clinical entity with different backgrounds, demonstrating heterogeneous pathophysiological bases.

Early diagnosis of the triggering cause and the consideration of associated risk factors make a difference in patient outcomes.

The syndrome usually resolves over days to weeks, being the triggers usually identifiable, patients often suffer from comorbidities that may predispose them to develop PRES, being AKI/CKD one of them.

It is therefore important to consider PRES as a differential diagnosis in patients with acute or chronic renal disease, with or without RRT that are suffering from neurological symptoms.

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Suicidal Erythrocyte Death in Hemodialysis Patients

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Background: Even though anemia in end stage renal disease (ESRD) results mainly from the lack of erythropoietin, compelling evidence points to the contribution of accelerated erythrocyte death (eryptosis). Eryptosis is characterized by phosphatidylserine (PS) exposure at surface, cell shrinkage and cell membrane scrambling. In ESRD, eryptosis may be stimulated both by uremic toxins and the mechanical stress induced by hemodialysis. In this study, we investigated the possible difference in terms of eryptosis level between healthy subjects and patients undergoing hemodialysis (HD); furthermore, in this population we examined eryptosis level before and after hemodialysis session.

Materials and Methods: We enrolled 15 patients (4 females, mean age 65 ± 16 years, 33% with diabetes) undergoing chronic HD. Blood samples were collected prior to and after 4 h standard hemodialysis session. 15 healthy volunteers were recruited as control group (CTR). Measurements were made in freshly isolated erythrocytes. PS exposure was estimated from AnnexinV binding in flow cytometer.

Results: The percentage of AnnexinV binding erythrocytes reflecting the percentage of erythrocytes exposing PS at surface was

significantly higher (more than twice) in HD patients than CTR (2.2; IQR 1.2–4.1 versus 0.8; IQR 0.7–1.3; $p < 0.05$). The average forward scatter reflecting cell volume was significantly higher in erythrocytes from HD patients than in CTR. There was no statistically significant relationship between urea levels and eryptosis in HD patients. The percentage of AnnexinV binding erythrocytes and cell volume were measured prior to and after 4 h of HD: no significant differences were observed between predialytic and postdialytic eryptosis.

Conclusion: Our data suggest that HD may lead to a significant increase in eryptosis, but no differences in its level were observed before and after hemodialysis session. Although dialytic procedure is known to be responsible for cytokines and inflammatory mediators release, because of the interaction between blood and circuit lines and filters, it does not seem to induce eryptosis. Further studies are needed to compare different types of extracorporeal treatments.

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Haemolytic Uremic Syndrome – The Impact of Early and Targeted Intervention on the Course of Potentially Life-Threatening Disease

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A 30-year-old female was admitted with complaints about abdominal and back pain, nausea, and vomiting, bloody urine. These symptoms appeared 2 days prior hospitalization. On admission patient was suspicious to have renal colic due to nephrolithiasis. Patient history demonstrated that she had been hospitalized with similar complaints in UK four years ago – haemolytic uremic syndrome (HUS) was found and rapid improvement with plasma exchange and steroid therapy was achieved. Another episode was in her early childhood with spontaneous remission but there was lack of detailed information about this case. She had no relevant family history.

On admission her BP was 180/110 mm Hg, weight 75 kg, she had decreased renal function (creatinine 151 $\mu\text{mol/l}$; eGFR 37.18 ml/min MDRD), thrombocytopenia ($22 \times 10^3/\mu\text{l}$), haemolysis (LDH 2324 U/l; haemolysis test 0.26 g/dl; ref. range <0.05 g/dl). US of abdomen had no relevant finding.

Taking into account her past medical history and these results, a diagnosis of HUS was established. CVC was placed in femoral vein and urgent therapeutic plasma exchange (TPE) procedure was performed already within the first 4 hours after the admission. TPE was continued daily for the first week. During each session 0.5 plasma volume was exchanged to six units of fresh frozen plasma and crystalloids. Due to continued decrease of renal function she also had 2 sessions of IHD. Overall, she received 20 TPE procedures (daily for the first week, then 3–4–5 times a week.) as well as red blood cell and platelet transfusions, pulse steroids, ACEI. The duration of her treatment was one month with significant improvement – LDH reached to reference range, platelet count, Hb value gradually increased, renal function improved.

Thanks to our Lithuanian colleagues, patient had an opportunity for detailed genetic testing of complement for possible mutations. These tests revealed that she has a combined genetic predisposition to aHUS (1 mutation, 3 frequent risk variations), ADAMTS13 activity was 81% (on the background of TPE).

She is now in our close outpatient observation and is doing quite well already for one and a half year with stabile remission. She is on small dose of ACEI, her clinical condition is stable and all clinical analyses are in reference range, so there is no data of relapse until now.

The presentation aimed to show:

- Favourable outcome of a potentially life-threatening disease.
- The impact of very early diagnostics and intervention on the course of the disease.

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The Role of Endotoxin in the Setting of Cardiorenal Syndrome Type 5

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Lipopolysaccharide (LPS) or endotoxin, the major constituent of the outer membrane of Gram negative bacteria, plays a pivotal role in the pathogenesis of sepsis. It is able to activate the host defense system through the interaction with Toll-like receptor 4, thus triggering pro-inflammatory mechanisms. When the production of inflammatory mediators becomes uncontrolled and excessive, septic shock develops with multiple organ dysfunction, such as myocardial and renal impairment, which are hallmarks of cardiorenal syndrome type 5.

Cardiac dysfunction during sepsis consists of decreased cardiac contractility, impaired ventricular response to fluid therapy and progressive ventricular dilatation. Septic acute kidney injury (AKI) is characterized by renal arterial vasodilation and preserved overall renal blood flow, the so-called hyperemic AKI. Indeed, glomerular filtration rate and cellular perfusion have been demonstrated to decrease even if overall renal blood flow is increased. During combined acute cardiac and renal dysfunction, such as in sepsis, decreased cardiac output leads to reduced renal perfusion, which further aggravates sepsis-induced AKI. Endotoxin impairs glomerular filtration rate, as well as tubular function, with consequent fluid and electrolyte alterations. Consequently, fluid overload due to AKI can lead to acute heart failure, and metabolic acidosis can impair cardiac contractility and increase heart rate, thus worsening myocardial workload.

Based on this concepts, it is reasonable to antagonize and/or to remove endotoxin when treating patients with sepsis. A novel therapeutic system whereby polymyxin B is immobilized to a polystyrene-derived fiber (PMX-DHP) in a hemoperfusion device has been recently proposed in order to remove circulating endotoxin. Several trials of small cohorts of patients as well as case reports and case series reporting the efficacy of PMX-DHP in severe sepsis

have been published. Early identification of sepsis-associated AKI and heart dysfunction is mandatory to start therapy as soon as possible, thus improving clinical outcome.

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A Prospective Study of Burden and Outcome of Acute Kidney Injury from a Tertiary Centre in Singapore

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Aims: Acute kidney injury (AKI) among hospitalized patients imposes significant morbidity and mortality globally. AKI e-alert and AKI Care Bundle are proposed to allow early diagnosis and possibly improved outcomes. We sought to study the burden and outcome of diagnosed AKI and acute-on-chronic kidney disease (AoCKD) in our center with a view towards implementing AKI e-alert and AKI Care Bundle.

Methods: Data of patients diagnosed with AKI by KDIGO (Kidney Disease, Improving Global Outcomes, 2012) criteria from 15th July to 22nd October 2016 in Singapore General Hospital were prospectively collected from electronic medical records and clinical notes. Patients with estimated glomerular filtration rate (eGFR) of <15 ml/min were excluded. Patients were followed up till 90 days after AKI diagnosis.

Results: Our 100-day prospective study included 432 episodes of AKI in 405 unique patients, with an AKI incidence of 2.2%. Majority of patients were male (58%), Chinese ethnicity (69.1%) and median age at AKI was 68 years (IQR, 56–76). Among critically ill patients, 140 AKI episodes (32.4%) were diagnosed in acute care units. Seventy-five percent of AKI episodes developed during admission in a non-Renal specialty. Median baseline serum creatinine and eGFR were 141 µmol/L (IQR, 93–200) and 42 ml/min (IQR, 27–71) respectively. Thirty-seven percent of patients had underlying CKD stage 3 to 4. Median creatinine at AKI diagnosis was 259 µmol/L (IQR, 193–363). Renal consultations were initiated at KDIGO Stage-1, 2 and 3 in 59.3%, 24.7% and 16%, respectively. One hundred and seventeen (28.8%) patients received renal replacement therapy (RRT), of which 57% had continuous renal replacement therapy. Mortality with AKI was 18.7% during hospitalization. Ninety-day survival post AKI diagnosis was 72.2%.

Conclusion: The high incidence and increased mortality of AKI and AoCKD dictates the need for early prevention and intervention, suggesting a potential role for AKI e-alert and Care Bundle in earlier diagnosis and mitigating reversible risk factors of AKI.

Factors Related with AKI After Cardiac Surgery

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Background: Acute kidney injury (AKI) is a prominent complication after cardiac surgery and it is associated with increased morbidity and mortality. The incidence of AKI ranges from 1–30% in patients with cardiac surgery and it is associated with 20% mortality. AKI is caused by a variety of factors. Lacking effective therapies, risk factor modification may offer a means of preventing this complication. The current study now aims to identify and determine the prognostic importance of such risk factors.

Methods: We performed a retrospective single-center cohort study of patients who underwent an on-pump CABG or an open-chamber valve procedure (valve repair or replacement) between January and December 2014. Patients with and without AKI were identified using the KDIGO guidelines definition. The inclusion criteria were patients with on-pump CABG or an open-chamber valve procedure older than 18 years. The exclusion criteria were chronic kidney disease (CKD) stage 5, patients with RRT before the surgery and minimal surgical procedures. Clinical characteristics at admission and in the day of the surgery were collected. Statistical analysis was performed with the IBM statistics package SPSS for Mac version 21 (SPSS, Chicago, Ill, USA). Variables were presented as medians (interquartile range) for continuous data and as the number of patients and percentages for categorical parameters. Comparisons between No-AKI and AKI groups were made by using X² or Fisher's exact test for categorical variables and Mann-Whitney U test and Student's t test for quantitative parameters. To identify independent variables related with AKI, a binomial logistic regression analysis was performed. The goodness of fit of the model were assessed using the Hosmer-Lemeshaw statistics, the sensitivity and specificity of the model and the area under the receiver operating characteristics curve (AUROC) of the model.

Results: 258 patients were enrolled, among them 101 (39.1%) developed AKI during the CU stay. The variables that differed significantly between No AKI and AKI groups were: (a) age [67 versus 73 years, $p < 0.0001$], (b) history of high blood pressure [29.3% versus 80.2%, $p < 0.0001$], (c) history of diabetes mellitus [22.3% versus 70.3%, $p < 0.0001$], (d) Euroscore 2 [6 versus 7.5, $p < 0.0001$], (e) Cleveland score [2 versus 3, $p < 0.0001$], (f) time on-pump [84 versus 106 minutes, $p < 0.0001$], Hemoglobin [13 versus 11 g/dL, $p < 0.0001$], (g) Length of stay in CU [2 versus 4 days, $p < 0.0001$]. In the binomial logistic regression model: age in years (OR = 1.042, $p = 0.008$), Cleveland score (OR = 1.854, $p < 0.0001$) and the time on-pump in minutes (OR = 1.009, $p = 0.035$) were associated with an increase in likelihood of develop AKI after the cardiac surgery. The AUROC of the model was 0.789.

Conclusion: The increase of the time on-pump, the worsening on the Cleveland score and the increase of age could be factors related with an increase in likelihood of develop AKI after the cardiac surgery.

Accelerated Neurological Recovery in a Patient with Miller Fisher Syndrome(MFS) Treated by Plasma Immuno Adsorption (IA)

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Background: MFS is an infrequent variant of Guillain-Barré Syndrome. The diagnosis is made on clinical ground, based on the triad of ataxia, areflexia and ophthalmoplegia. Detection of anti-GQ1b antibodies is the serological confirmation. MFS has a self-limiting clinical course. However, complete recovery may require up to six months. Causative factors are infections of the upper respiratory or the gastrointestinal tract provoked by *Campylobacter jejuni*, Cytomegalovirus, EBV, *Mycoplasma pneumoniae*, influenza viruses. MFS may mimic botulism, poliomyelitis, poisonings. The treatment consists of i.v. immunoglobulins, plasmapheresis (PEX), steroids, and if necessary ventilatory support and parenteral nutrition.

Case Presentation: a 46 years-old Caucasian male was admitted to Neurology Department for ataxia, areflexia, ophthalmoplegia and generalized fatigue. He was unable to ambulate and had bilateral incomplete deficiency of the III cranial and complete deficiency of the VI and IX cranial nerves. He reported frequent upper respiratory tract infections during the preceding year. One month before admission he presented visual disorders, while the day before he complained of perioral and upper left limb numbness associated to dysphonia and rhinolalia, later on. The patient manifested also arterial hypertension. At the admission the neurological picture included: eyelid ptosis, diplopia, dysphagia, impaired balance, clumsiness, constipation. The brain CT, MNR and electrophysiological study were normal, also echocardiogram and chest Rx did not show alterations. Laboratory testing showed mild leukocytosis and increase of C-reactive protein, while metabolic panel, TSH, and cardiac and tumor markers were normal. Throat swab, VDRL, TPHA, culture of liquor, toxoplasma and virus indirect serology and C-reactive protein to viral DNA CSF were negative. CSF didn't show cytoalbuminologic dissociation. Common autoimmunity tests were negative. Therefore, an empirical PEX treatment was started. After three sessions of PEX the clinical picture did not improve. Since anti-GQ1b antibodies were positive, the diagnosis of MFS was evident and we switched to IA with TR-350 filter (BBraun, Germany). After two treatments a marked improvement of clinical conditions were found, with regression of eyelid ptosis, ataxia, areflexia, dysphonia and dysphagia. After a total of seven sessions of IA the patient had recovered almost completely and was discharged.

Discussion: In this case of MFS, a prompt treatment with IA and TR-350 filter induced a rapid clinical recovery of neurological symptoms. One month after the onset, test for anti-GQ1b anti-

body was negative, the patient reported a complete resolution of physical discomfort and had returned to his normal work activities. The ocular symptoms, which were the first to appear, resolved last.

Conclusion: In conclusion, treatment of MFS with IA may speed-up the clinical recovery of neurologic symptoms and may represent a valid therapeutic alternative to PEX or iv immunoglobulin infusion.

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Sinusoidal Obstruction Syndrome (SOS) after Solid Organ Transplantation

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Background and Aims: Sinusoidal obstruction syndrome (SOS), endothelial cell membrane obstruction in the terminal hepatic venules and sinusoids, is a rare complication after solid organ transplantation and it is associated with a high mortality rate. Early initiation of appropriate therapy to improve clinical outcomes is essential when considering the diagnosis of SOS. We present two cases with biopsy proven SOS after solid organ transplant and a review of literature, that illustrate difficulties in diagnostic work up and treatment.

Methods: All cases of SOS after solid organ transplant in a 10-years period were identified by an electronic search for defibrotide use and review of all obduction reports. Furthermore current knowledge on diagnostic strategy, treatment and prognosis was summarized from a systematic search of literature.

Results: A schematic overview of cases is presented in figure 1.

Case 1: A 49 year old male, 4 months after kidney-pancreas transplantation, was admitted to the ICU because of tacrolimus toxicity induced diminished mental status. Also jaundice, ascites and right upper quadrant pain were present. Other causes of hyperbilirubinemia were excluded. SOS effective treatment with defibrotide was initiated, unfortunately leading to gastro-intestinal bleeding and death. Obduction confirmed SOS.

Case 2: A 44 year old female, 9 years after kidney-pancreas transplantation, was admitted to the ICU because of catheter related septic endocarditis, with good response on antibiotic treatment. She developed ascites, jaundice and GI bleeding due to hypertensive gastropathy and portal hypertension. SOS was diagnosed by liver biopsy, but due to persistent bleeding despite a TIPPS, defibrotide was contraindicated and patient died under supportive care.

In literature SOS is rarely described after solid organ transplant (n = xxx/yyy) and mostly associated with immunosuppressive medication with high mortality rate. The pathogenesis is

poorly understood and the diagnostic work up comprises of excluding other causes of hyperbilirubinemia, measurement of veno-portal pressure gradient and liver biopsy. Successful treatment with defibrotide, solumedrol and liver transplantation are described.

Conclusion: SOS occurs also after solid organ transplantation and it has been associated with a high mortality. Therefore an accurate and prompt diagnosis of SOS is essential for early initiation of appropriate therapy to improve clinical outcome.

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Impact of Hypoalbuminemia on Survival of Patients with Acute Renal Injury

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Introduction: Hypoalbuminemia is associated with inflammatory and malnutrition states that may increase the risk of mortality, especially in patients undergoing acute kidney injury (AKI). This study aimed to evaluate the impact of hypoalbuminemia on the survival of patients with AKI 30 days after discharge.

Methods: Observational and retrospective study of 316 patients admitted for AKI (elevation of serum creatinine by at least 0.3 mg / dL or 1.5–2x) in the Department of Nephrology. Demographic variables, the Charlson comorbidity index (CCI) and laboratory data were collected on admission, at discharge, and one month later. Patients were grouped according to serum albumin at admission: group 1 (≤ 3 g/dL) (n = 200; 63%) and group 2 (> 3 g/dL) (n = 116; 37%).

Results: A total of 316 patients (53% male) with a mean age of 75 ± 14 (min-max: 18–98) years were included; 37% (n = 117) were older > 65 years and 44% (n = 140) were very old (> 80 years); 23% were institutionalized. Of the 316 patients admitted, 192 (61%) underwent hemodialysis (HD) during hospitalization and 83 (43%) were still on dialysis 30 days after discharge ($p \leq 0.001$). When comparing both groups, group 1 consisted of older patients (76 ± 14 vs. 71 ± 14 years, $p = 0.006$), especially those aged > 80 years (53 vs. 30%, $p \leq 0.001$), residing in nursing homes (36 vs. 23%, $p = 0.019$) with longer hospitalizations (16 ± 12 vs. 13 ± 11 days, $p = 0.016$), higher C-reactive protein (11 ± 9 vs. 6.9 ± 7 , $p = 0.004$) and more infections (74 vs. 26%, ≤ 0.001). There were no differences in baseline serum creatinine and on admission or on comorbidities based on CCI. Both groups required dialysis (63 vs. 58%, $p = \text{NS}$) during hospitalization at a mean time of 3 ± 1 days ($p = \text{NS}$), but group 1 had a lower recovery of renal function (27 vs. 52%, $p = 0.036$), a higher hospital mortality rate (19 vs. 5%, $P \leq 0.001$) and greater dependence on dialysis (59 vs. 43%, $p = 0.028$) at discharge. In a 30-day follow-up, group 1 presented a superior rate of renal recovery (20 vs. 0%, $p \leq 0.001$), lower mortality (4 vs. 10%, $p = 0.04$) and dialysis dependence (80 vs. 100% $p < 0.018$). However, overall mortality was higher in group 1 (22 vs. 9%, $p = 0.023$). Infectious (respiratory and urinary) processes accounted for the majority of deaths in both groups.

Fig. 1. Schematic overview of cases (for Abstract no 18).

Conclusion: Hypoalbuminemia, present mainly in the elderly and institutionalized population, increased mortality and dialysis-dependence in patients submitted to AKI, especially during hospitalization. This fact alerts us to intervene in advance avoiding any kind of renal insult that may trigger the need for dialysis.

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Acute Kidney Injury in Patients with End-Stage Liver Disease: Prognostic Factors for Renal Function and Patient Survival

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Introduction: Acute kidney injury (AKI) is a frequent complication in patients with end-stage liver disease with an incidence of 20% in hospitalized cirrhotic patients and a mortality

that can reach 80%. The aim of this study was to describe the incidence and different causes of AKI in patients with end-stage liver disease, analyse prognosis of renal function according to the etiology of liver disease and AKI, compare patient survival in hepatorenal syndrome (HRS) versus other causes of AKI and study the predisposing factors for the absence of recovery from AKI.

Methods: A retrospective study was conducted that included 92 patients hospitalized at our medical center between July 2013 and March 2016, with end-stage liver disease and an inpatient referral to the nephrology department for AKI after matching AKIN criteria. The following variables were analysed; demographic variables, etiology of liver disease and AKI, time of nephrology consultation, biochemical values (basal and subsequent controls for creatinine and estimated glomerular filtration, albumin, INR, serum and urine and bilirubin), treatment (fluid therapy, diuretics, vasoactive drugs, albumin infusion), time for recovery from AKI, start of dialysis and death were collected.

Results: Among the 92 recruited patients, 70 were males (76%), mean age of 65.6 ± 13.7 years. HRS was seen in 25 patients (27.2%), while volume depletion/sepsis was observed in 24 patients (26.1%) and hydropic decompensation in 28 patients (30.4%), 5 of them with associated heart failure, and 15 had other causes of AKI. As for the etiology of liver disease, 36 patients had alcoholic cirrhosis and 36 HCV-related cirrhosis (39.1% respectively), 11 had other causes for liver disease (12%) (4 with cancer related pathology, 3 with HBV-related cirrhosis, 2 with autoimmune liver disease, 2 with fulminant hepatic failure) and in 9 cases the etiology was unknown (9.8%).

At the end of follow-up, 57 patients (62%) had died, and 5 (5.4%, all HCV positive) were started on hemodialysis (HD). Recovery from AKI was seen in 61 cases (66.3%).

Recovery from AKI was higher in volume depletion/sepsis group compared to HRS (91.7% vs. 44%, $p = 0.005$). No differences in kidney function prognosis were found according to the etiology of liver disease.

AKI due to HRS had a higher overall mortality compared to the rest of causes (80% vs. 55%, $p = 0.029$). Median survival of patients with HRS was 31 ± 21.7 days, compared to 367 days for patients with volume depletion/sepsis, 495 ± 283.4 days for patients with hydropic decompensation and 131 ± 103 days for other causes of AKI.

Median survival was of 31 ± 21.7 days for patients with HRS vs. 289 ± 194.6 days for other causes of AKI ($p = 0.04$).

Patients with oliguric AKI had a median survival of 48 ± 26.9 days versus 495 ± 231.7 days for patients with non-oliguric AKI ($p = 0.045$).

Comparing the group of surviving vs. deceased patients, we found statistically significant differences in the following biochemical parameters: urine sodium (49 ± 30.6 mmol/l vs. 35.1 ± 26.6 mmol/l, $p = 0.037$) and diuresis (897 ± 631 ml/day vs. 617 ± 491 ml/day, $p = 0.048$).

Univariate logistic regression was also performed, obtaining as risk factors for mortality; non-recovery from AKI, urine sodium and HRS. In the multivariate logistic regression analysis only non-recovery from AKI was shown to be an independent risk factor for mortality (HR 33.99, $p = 0.001$).

Conclusions: The most frequent cause of AKI in end-stage liver disease is hydropic decompensation, while HRS has shown to have the worst prognosis.

The failure to recover from AKI is an independent risk factor for mortality in patients with advanced liver disease. However, mortality rates are high in this group of patients even in those who recover from AKI.

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Factors Related with Effective Discontinuation of CRRT in ICU

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Background: Acute Kidney Injury is a frequent complication in patients admitted to Intensive Care Units (ICUs). Approximately 25% of these patients deteriorate clinically and are unable to maintain adequate homeostasis, eventually requiring continuous renal replacement therapy (CRRT) in many cases until adequate metabolic control and fluid balance are attained. However, when clinical improvement occurs, the ideal mode of weaning patients from CRRT remains unclear.

Fig. 1. The area under the receiver operating characteristics curve of urine output for effective discontinuation of CRRT was 0.804 and the highest accuracy for UO was 720 mL/day (for Abstract no 21).

Table 1. Binomial logistic regression model for effective discontinuation (for Abstract no 21)

	<i>p</i> value	OR	95% CI	
			Lower	Upper
Urine Output (ml/kg/h) ^a	0.000	14.957	3.396	65.871
PaO ₂ /FiO ₂ ratio ^a	0.010	1.009	1.002	1.016
Cardiovascular SOFA score ^a	0.004	0.479	0.288	0.796
BMI ^b ≥30kg/m ²	0.046	5.643	1.032	30.866

OD, odds ratio; CI, confidence interval; BMI, Body Mass Index.
^a Within 24 hrs of CRRT cessation. ^b ICU admission.

AuROC (95% CI): 0.919 (0.848–0.990), Goodness-of-fit *p* value: 0.08.

Methods: We performed a retrospective single-centre cohort study of AKI patients treated with CRRT between 2015 and 2016 in an ICU of an Italian hospital. Clinical characteristics at admission, the day of CRRT initiation, and the day before CRRT discontinuation were analysed. Patients were classified into two groups: 1) *effective discontinuation group*, defined as independence from RRT for at least 14 days after CRRT discontinuation; and 2) *ineffective discontinuation group*, which included patients who required CRRT resumption therapy within 14 days along with those who were dialysis-dependent at discharge at ICU or whose reason for CRRT termination was death. Factors associated with effective discontinuation were identified by binary logistic regression.

Results: A total of 77 patients were enrolled, of whom 37 (48.1%) were classified in the effective discontinuation group. Increased urine output (OR = 14.957, *p* < 0.0001) and PaO₂/FiO₂ ratio (OR = 1.009, *p* = 0.010) measured 24 hrs before CRRT discontinuation along with body mass index (BMI) ≥30 kg/m² (OR = 5.643, *p* = 0.046) were associated with increased likelihood of effective discontinuation while increased cardiovascular SOFA score (OR = 0.479, *p* = 0.004) was associated with a reduced likelihood.

Conclusions: Relatively high urine output measured 24 hrs before CRRT termination is associated with successful discontinuation of CRRT. Additional factors potentially influencing the effectiveness of termination are PaO₂/FiO₂ ratio, BMI, and cardiovascular SOFA score. The association between high BMI and successful discontinuation requires further evaluation.

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Characterization of Type I and II Cardiorenal Syndrome Patients Receiving Peritoneal Dialysis in a Population from Bogotá – Colombia

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Background: Chronic heart failure (CHF) that involves renal functionality is denominated cardiorenal syndrome (CRS). Peritoneal dialysis (PD) offers a therapeutical alternative with positive impact in heart functionality, hospitalization rates, clinical symptoms and mortality.

Objectives: describe the evolution of renal residual function and mortality in CRS patients treated with PD as a non uremic indication in a dialysis center in Bogotá – Colombia between 2013 and 2016.

Method: We performed a retrospective study. We included patients with non uremic indication for PD since 1/08/2013 until 1/08/16. We collected renal function data at the beginning and at the end of the followship from electronic clinical stories (RENIR – VERSIA™) from one dialysis center from RTS Bogotá.

We used STATA® 12.0 to perform the statistical analysis. We estimated the speed of loss of residual renal function (RRF) based in a linear model of regresión coefficient. Mortality rate was evaluated by Kaplan Meier method.

Results: We evaluated data from 16 patients, with mean age of 71 years old, with average ejection fraction about 29%± 12.7; whose mean time on PD therapy was 10.9 months.

We calculated a decrease rate of RRF of 0.75 ml/min/1.73 m² by each 1.46 months. Mortality rate was 41.61% and one-year survival was 68%. The main cause of death was acute myocardial infarction.

Conclusions: average age of our population is higher of the previously described by other authors. The lowering (loss) of RRF is higher than expected in PD for uremic indication.

There is an improvement of mortality rates in our population treated with PD when compared to the general CHF population.

Cooling Related with CRRT: Frequency and Hemodynamic Effect

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Background: The use of extracorporeal circuits for renal support can influence changes in body temperature. There have been described deleterious effects of hypothermia in the critical patient so different devices are used to avoid the cooling associated with CRRT. However, the direct hemodynamic effect and the ideal temperature level have not yet been extensively studied. The aim of this study is to describe the frequency and hemodynamic effect of cooling in the first 24 hours of CRRT initiation.

Methods: This is a retrospective observational study of 197 patients who required CRRT as a modality of renal support in one academic hospital of Bogotá, Colombia. We describe demographic, clinical and biochemical previously to CRRT initiation and 24 h after it. The primary outcome was the change in temperature, hemodynamic variables and vasopressor support within 24 hours of starting therapy. To compare changes in temperature and mean arterial pressure at time 0 of the initiation of therapy and the first 24 hours were used Wilcoxon signed rank test.

Results: The mean age was 69 years (SD 18.1), of which 64% were male, 48% of patients have APACHE II score >28, main related ICU diagnosis at the time of CRRT initiation were sepsis (28%), cardiovascular shock (23%) and respiratory failure (20%). Main dialysis criteria were AKI Rife F (36%), multiorgan dysfunction (21%), septic AKI (19%). Mean initial fluid balance was 5045 ml (SD 12865). At CRRT onset (T0) the median temperature was 36.3°C (IR 1), median arterial pressure was 84 mm Hg (IR 21), median heart rate was 87 bpm (IR 25.5), CVSOFA <2 (27%) CVSOFA 3 (40%) and CVSOFA 4 (33%). 24 hours after CRRT onset (T24) the median temperature was 35.9°C (IR 1.4), median arterial pressure was 89 mm Hg (IR 24), median heart rate was 84 bpm (IR 30), CVSOFA <2 (31%) CVSOFA 3 (38%) and CVSOFA 4 (31%). When evaluating the temperature at the beginning of the therapy and comparing it at 24 hours, the Wilcoxon test of the signed ranges showed a significant decrease in temperature ($p < 0.001$) and an increase in mean arterial pressure ($p = 0.03$), 52% of the population had a decrease greater than 0.3° C in the first 24 hours of therapy, there was no evidence of a decrease in the number of vasopressors or an improvement in cardiovascular SOFA. Hospital discharge mortality was 63% and dialysis dependence 12%.

Conclusions: The initiation of continuous renal replacement therapy is associated with a significant decrease in patient temperature at 24 hours, in addition to improvement in mean arterial pressure. Prospective studies are needed to explore the impact of temperature changes in CRRT patients in clinical outcomes.

Timing of Renal Replacement Therapy Among Critically Ill Patients with Acute Kidney Injury

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Introduction: Acute kidney injury is a common complication in critically ill patients and increases mortality rate. Despite continued use of renal replacement therapy in intensive care units (UCI), it is still unclear the appropriate timing for its beginning. Thus, our aim was to present the experience of an UCI in timing of renal replacement therapy initiation.

Material and Methods: Retrospective analyze of all critically ill patients with acute kidney injury submitted to renal replacement therapy between January 2009 to December 2013. We collected clinical, laboratorial, time to start dialysis and scores of mortality prediction.

Results: We included 119 patients. Median value for urea at time of dialysis beginning was of 156 mg/dL. We considered group 1 of early beginning, those with urea <156 mg/dL ($n = 61$) and group 2 of later beginning ≥ 156 mg/dL ($n = 58$). Mean age was of 63.4 years, the majority of male gender (52.9%). Group 1 delayed 2.5 days for start dialysis and group 2, 2.8 days ($p = 0.674$). Creatinine and potassium values were superior in group 2 compared to group 1 (6.4 mg/dL and 5.0 mEq/L vs. 3.8 mg/dL and 4.7 mEq/L; $p > 0.001$ and $p = 0.06$; respectively). Urine output was not different between groups (526 vs. 914 mL) ($p = 0.206$), but oliguria represented an indication for dialysis in 70.5% of cases in group 1, compared to 56.9% of group 2. Patients who initiated dialysis earlier presented similar respiratory failure rates (ARDS: 50.8 vs. 39.7%; $p = 0.221$) and also similar period of ventilatory support compared to later group: 10.4 vs. 7.7 days ($p = 0.157$). Patients of group 2 were more severe (score Apache II: 30.7 vs. 27.7; $p = 0.03$). However, mortality rate was not different between groups (60.3 vs. 47.5%; $p = 0.161$). Metabolic acidosis ($\beta = 1.41$; $p = 0.029$), anuria ($\beta = 1.73$, $p = 0.034$) and obesity ($\beta = 1.79$; $p = 0.017$), were independent predictors of early start of dialysis.

Conclusions: Timing in renal replacement therapy had no impact in mortality rate of critically ill patients with acute kidney injury.

Factors Related with Renal Recovery After AKI in ICU: Nephrocheck Biomarker Additional Value

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Background: Non-recovery of kidney function following an episode of acute kidney injury (AKI) is a major morbid event with long-term implications for patients and health resources based in short term mortality, progression to CKD and derived problems of chronic dependence of renal replacement therapy. The long-term rates for complete or partial recovery of function are not well described and data related to the progression to chronic kidney disease (CKD) are conflicting.

There are several definitions of renal recovery. The ADQI group affirmed: the ideal definition for recovery should quantify lost pre-existing kidney function as well as current residual kidney function and reserve, identify when recovery is complete, and provide prognostic information; but no standardized definition of recovery from AKI exists.

In the last years the use of biomarkers are becoming a diagnostic tool of clinical practice to predict high risk for AKI.

One of those biomarkers, insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2), are able to identify patients at high risk for AKI, the basis of the Nephrocheck™ (NC) test.

The aim of the current study is to identify factors related to early recovery and non-renal recovery in patients with AKI in ICU.

Methods: We performed a prospective single-centre cohort study of patients with AKI admitted in ICU between June 2016 and March 2017 in an Italian hospital. We defined AKI using the KDIGO criteria 2012. NC at admission and clinical characteristics during ICU stay were analysed. Patients were classified in two groups: 1) Early recovery group, defined as patients with AKI reversal within the first 7 days of reaching stage 1, 2 or 3; 2) Non-recovery group, which included patients with persistent AKI after the first 7 days, dialysis-dependence or death. Comparisons between groups were performed by using χ^2 or Fisher's exact test for categorical variables and Mann-Whitney U test and Student's *t* test for continuous parameters. Competing risk analysis using the Gray's test was performed.

Results: A total of 163 patients were enrolled, among them 88 (54%) were classified in the early recovery group. Age, diabetes, fluid balance, cardiovascular SOFA score, serum creatinine on admission and AKI stage 2 and 3 were significantly higher and urine

output, PF ratio, bicarbonate were significantly lower in the non-recovery group. NC value was non-significantly higher in the non-recovery group ($p = 0.113$), 0.82 (0.21–2.65) versus 0.89 (0.39–5.14) (ng/ml)²/1000, (median, IQR). Nevertheless, the proportion of NC >2 (ng/ml)²/1000 was significantly higher in the non-recovery group, 41.3% versus 26.1% in the other group ($p = 0.040$). The competing risk analysis revealed an increased likelihood of early recovery in patients with NC ≤2 (ng/ml)²/1000, ($p = 0.014$), in contrast to patients with NC >2 (non-significant).

Conclusion: NC >2 (ng/ml)²/1000 is associated with lower rate of renal recovery. Additional factors potentially influencing the renal recovery are age, diabetes, urine output and fluid balance within 24 hrs of ICU admission, cardiovascular SOFA score and AKI state. The association between NC and renal recovery requires further evaluation.

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Spontaneous Perirenal Hemorrhage in Hemodialysis Patients Treated with Selective Embolization: A Case Series

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Background: Spontaneous perirenal hemorrhage (SPH) or Wunderlich syndrome, is a rare but potentially life-threatening condition. This condition was first discovered and described by Bonet in 1700, and was initially clinically described as a spontaneous renal capsule apoplexy by Wunderlich in 1856 [1]. It is characterized by an unexpected bleeding in the kidneys and usually presents as an abdominal pain. The bleeding occurs into the sub-capsular and perirenal spaces. Renal tumor and cysts followed by vascular disease are the most common causes [2]. In recent years, many cases of SPH have been reported, especially in hemodialysis (HD) patients, and it seems to be independent of the original renal disease. Angiography and more recently selective renal arterial embolization are emerging as effective modalities for the diagnosis and treatment of SPH [3].

Objective: To describe the clinical characteristics and to identify risk factors of SPH in HD patients.

Case Presentation: In our experience, we report a total of three cases of SPH in HD patients treated with selective renal arterial embolization. Patient characteristics are described in Table 1. All three were female, between 37 and 54 years of age and were undergoing MHD for end stage renal disease (ESRD). Two of our patients presented with left flank or abdominal pain after termination of HD therapy, while the third patient presented with left abdominal pain during the dialysis session. All patients received anti-coagulation therapy for HD, heparin in one case and low-molecular-weight heparin in the others. We didn't find any abnormal levels of coagulation index. These patients were diagnosed using CT and two of them were diagnosed with acquired cystic kidney disease (ACKD). Selective renal arterial embolization was

Table 1. Patient characteristics (for Abstract no 26)

Case	1	2	3
Age (years)	37	54	45
Sex	Female	Female	Female
Etiology	Diabetic nephropathy	Chronic Glomerulonephritis	Hypertensive nephropathy
History of dialysis (months)	60	96	6
CT findings	ACKD	ACKD	Hamartoma?
Symptom	left flank pain	left abdominal pain	left abdominal pain
Anticoagulant	LMWH	LMWH	Heparin
Position	Left kidney	Left kidney	Left kidney
PLT (10 ⁹ /l)	114	213	152
PT (s)	14.6	13.7	13.5
PT (INR)	1.42	1.09	1.48
APTT (s)	42.3	32.7	30.5
Calcium (mmol/l)	2.07	2.59	2.23
Treatment	SRAE	SRAE	SRAE
Outcome	Required embolization twice	Resolution of the bleeding with embolization	Resolution of the bleeding with embolization

LMWH, low-molecular-weight heparin; PLT, Platelets; PT, Prothrombin time; INR, international normalized ratio; APTT, Activated partial thromboplastin time; ACKD, acquired cystic kidney disease; SRAE, Selective renal arterial embolization.

performed considered active bleeding. One of these patients needed a second embolization because bleeding did not stop. The other two had hemoglobin stabilization and resolution of the bleeding and abdominal symptoms.

Conclusion: We are aware that HD patients have elevated risk of bleeding related complications, additionally the presence of an acute abdominal pain increases the suspicion of SPH as a possible cause. ACKD can be considered one of the possible risk factors for SPH in long-term HD patients. Interventional treatment for kidney injury is suitable and useful for active bleeding in most cases.

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SNP Profiling of Renal Allograft Recipients with Acute Rejection

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Background: Transplant outcomes exhibit substantial inter-individual variability among patients receiving the same immunosuppressive therapy. Single-nucleotide polymorphisms (SNPs) in genes involved in immune responses and in the pharmacokinetics/pharmacodynamics of immunosuppressive drugs are reported to be linked to acute rejection (AR) following kidney transplantation.

The aim of the study was to determine the SNPs profiles of ABCB1/MDR-1, UGT1A9, IMPDH2, IL-10 and TNF- α genes associated with the acute rejection event in renal allograft recipients.

Methods: DNA was extracted from whole blood samples collected in 3 experimental groups; Case: kidney transplant patients with AR event(s), Control I: kidney transplant patients without AR event, Control II: healthy blood donors. Acute rejection defined as a rapid and unexplained rise in serum creatinine was biopsy-proven. 19 SNPs were analyzed by Sanger Sequencing. Statistical analysis of allele and genotype frequencies and trend test were per-

formed between Case vs. Control I; Transplant (Case+Control I) vs. Control II; Case vs. Control II groups.

Results: We enrolled 220 individuals (63 females and 157 males): 70 healthy blood donors, 109 transplant patients without AR and 41 transplant patients with AR; the median age (p25th-p75th) was 50 (42–62), 55 (48–62) and 49 (41–54) respectively. The observed allele frequencies in the Control group are in line with ones reported from Europe indicating that the studied population is representative.

Statistically significant differences only by the comparison of Case and Control II groups are found for 2 SNPs of ABCB1/MDR1, one of which is also not in Hardy-Weinberg equilibrium (HWE).

Conclusions: Certain allele variants of ABCB1/MDR1 by modifying the effectiveness of the drugs may compromise the success of the immunosuppressive therapy and put patients at higher risk to reject the new organ. Patients with specific alleles for these SNPs are more prone to have AR events. Therefore screening for these SNPs before transplantation would help clinicians to more accurately personalize medications to avoid graft rejection.

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Acute Kidney Injury and Multiple Myeloma – A 10 Year Single Center Experience

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Introduction: Multiple myeloma (MM) is characterized by the neoplastic proliferation of plasma cells producing monoclonal immunoglobulin. It represents 1% of all cancers and 13% of hematologic malignancies. AKI is a common complication of MM, being present in about 50% of the patients at MM presentation and up to 5% require dialysis treatment. Recovery of renal function is more predictive of survival than the hematologic response to chemotherapy [1].

Aim: Evaluate the clinical profile of patients with AKI and MM and determine possible survival predictor factors.

Materials and Methods: We performed a single-centre retrospective analysis of the patients admitted between 2005 and 2014 in a Nephrology department with AKI and MM.

Results: A total of 46 patients were selected, with 54% being of feminine gender and mean age of 72.9 (65.6–80.6) years. The diagnosis of MM was already known in 44% of the patients and 68% had CKD. Admission mean creatinine was 6.6 (4.1–9.3) mg/dl and about 75% of the patients had hypercalcemia. During hospitalization 22 patients (48%) needed renal support therapy (RST) all of them with hemodialysis. In table 1 characteristics and outcomes in RST and No-RST patients are presented.

From the cox analysis performed, the factors that independently predicted death were: age (HR = 1.051; P = 0.024); RST need during the hospitalization (HR = 4.186; P = 0.013); presence of non-IgG mIg (HR = 4.683; P = 0.031) or solely light chain (HR = 5.303; P = 0.033) versus IgG mIg and admission hypoalbuminemia

at admission (<3 vs. ≥3 g/dl) (HR = 7.036; P = 0.001). Mean survival after the diagnosis of MM was 1.81 years. Mean survival after AKI was 1.55 years for patients that didn't need RST and 0.18 years for patients that needed RST (P = 0.042).

Conclusion: RST in patients with AKI and MM was frequent, particularly in those with a high serum M protein and it was associated with a statistically significant worse survival on these population.

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Extracellular Vesicles Induce Renal Tubular Cells Apoptosis, Oxidative Stress and Functional Abnormalities in Patients with an Acute Decompensation of Cirrhosis

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Introduction: Acute decompensation (AD) of cirrhosis is the main cause of hospitalization in patients with cirrhosis and patients with AD may develop acute-on-chronic liver failure (ACLF). Acute kidney injury is common in these patients. Recent findings suggest that splanchnic arterial vasodilation cannot fully explain organ dysfunction in these patients. Extracellular vesicles (EVs) are involved in many important biological processes as well as in disease pathogenesis. The origin and the role of EVs in the pathogenesis of liver disease is poorly recognized.

Aims: The aims of this study were: a) to characterize plasma EVs isolated from patients with compensated cirrhosis (CC), AD, ACLF and healthy subjects, b) to study the *in vitro* effects of isolated EVs on renal tubular cells (RTCs).

Material and Methods: Demographic, clinical and laboratory features of 12 CC patients, 13 AD patients, 11 ACLF patients and 12 healthy subjects were collected. Plasma EVs were extracted by ultracentrifugation and characterized in size and concentration by nanoparticle tracking analysis (NTA). Detection of EVs surface proteins, ROS productions in RTCs, protein expression in RTCs was performed by FACS analysis. Cytotoxic effects of plasma EVs on RTCs were assayed by XTT assay and TUNEL assay.

Results: Plasma EVs isolated from ACLF patients were more concentrated and bigger in size compared to healthy subjects (p =

Table 1. (for Abstract no 28)

	Total n = 46	No-RST n = 24	RST n = 22	p value
Age (years)	72.9 (65.6–80.6)	76.9 (64.5–81.2)	72.4 (65.6–75.2)	0.147
Feminine Gender (%)	54.3	58.3	50	0.571
DM (%)	20	8.7	31.8	0.071
HBP (%)	66.7	56.5	77.3	0.140
Dyslipidemia (%)	24.4	26.1	22.7	0.793
AKI + CKD (%)	67.5	68.4	66.7	0.906
Creatinine baseline (mg/dl)	2 (1–2)	1.62 (1–2)	2 (1–2.2)	0.281
Creatinine (mg/dl)	6.6 (4.1–9.3)	4.3 (3.3–7.3)	8.8 (6.1–12)	0.010
Urea (mg/dl)	139 (103–204)	135 (101–201)	150 (103–209)	0.598
Hgb (g/dl)	9.5 (8.7–10.6)	9.6 (8.8–11.5)	9.4 (8.0–9.8)	0.183
Leukocytes	7175 (5235–9733)	7220 (5525–10025)	7120 (4745–9732)	0.644
Platelets	1,70,000 (1,05,000–2,28,000)	1,93,000 (1,50,000–2,30,000)	1,35,000 (87,250–2,30,000)	0.099
Calcium (corrected to albumin)	2.81 (2.51–3.21)	2.76 (2.37–3.15)	2.88 (2.57–3.32)	0.358
Albumin	3.25 (2.84–3.87)	3.30 (2.92–4.01)	3.14 (2.74–3.46)	0.120
Proteinuria (g/d)	2.95 (1.91–5.92)	2.78 (2.15–4.17)	5.18 (1.72–8.46)	0.260
Sodium	136 (134–140)	138 (134–141)	135 (130–137)	0.038
Potassium	4.91 (4.24–5.60)	4.81 (4.07–5.21)	5.12 (4.44–6.04)	0.191
Phosphorus	1.47 (1.18–1.85)	1.39 (1.17–1.82)	1.65 (1.14–2.05)	0.192
Ig (n)				
– Kappa	7			
– Lambda	3			
– Ig A	7 (4k+3l)			
– Ig G	22 (17k+5l)			
– Ig D	4 (4l)			
– Ig E	1 (1k)			
Igs (n)				0.615
– Ig G (+ light chain)	22	21.7	23.8	
– Ig no-G (+ light chain)	12	56.5	42.9	
– Solely light chain	10	21.7	33.3	
Serum M Protein	1.7 (0.7–4.6)	1.5 (0.4–2.95)	5.2 (2.5–7.3)	0.003
(%)	22.1 (9.5–45.3)	11.9 (4.7–23.7)	52 (36.9–62.2)	0.006
Relation K/lambda				0.901
– Reduced	36.4	33.3	40	
– Normal	15.9	16.7	15	
– Increased	47.7	50	45	
% Urine albumin (Imune)	11.1 (5.7–28.5)	9.7 (4.2–30.5)	11.3 (6.2–28.9)	0.614
% Plasma cells medulla	16 (9–46)	15.5 (8.8–48.3)	19.5 (9–42.8)	0.385
Lytic lesions (%)	78.4	82.4	75	0.701
Previous MGUS (%)	21.4	25	16.7	1.0

0.002). Plasma EVs were mainly derived from platelets activated endothelium, as shown by the expression of (CD62E). The levels of CD62E were significantly higher in ACLF patients compare to CC patients and healthy subjects ($p = 0.011$ and $p = 0.004$, respectively). Platelet derived and monocytes derived EVs, as assessed by CD41, CD42b and CD14, were not found. CD40L levels, a receptor involved in lymphocytes T activation, were significantly higher in CC, AD and ACLF groups than in healthy subjects ($p < 0.02$). Plasma EVs from patients with AD and ACLF exerted a higher cytotoxic effects than EVs from healthy subjects and CC patients on RTCs ($p < 0.001$). Cells incubated with EVs from AD and ACLF patients showed an increase in apoptosis ($p < 0.001$) and ROS pro-

duction ($p < 0.001$), loss of albumin intake capabilities ($p < 0.001$) and reduction of ZO-1 expression ($p = 0.017$) compared to healthy subjects and CC patients.

Conclusions: EVs derived from activated endothelium may exerts an important role in the pathogenesis of acute kidney injury in patients with AD of cirrhosis and ACLF.

Nephrotoxicity and Traditional Chinese Medicine

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Traditional Chinese Medicine (TCM) has been practiced for thousands of years. In China, there are about 440,700 health care institutions including all levels of TM hospitals, general hospitals, clinics and health stations in both rural and urban areas with a total of 520,600 patient beds that provide Traditional Medicine (TM) services. About 90% of all general hospitals also include a TM department which provides TM services for all patients [1]. TCM is composed mainly of natural medicines, the effective ingredients are considerably complex and majority of them exhibit varying degrees of side effects. Some of these medicines are also known to cause nephrotoxicity, which is often overlooked by physicians and patients due to the belief that herbal medications are innocuous. There is a lack of recently published literature discussing this topic [2].

The TCM species known to be associated with nephrotoxicity:

1. Aristolochic acid: Aristolochiae, Radix Aristolochiae Fangchi, Caulis Aristolochiae Manshuriensis, Asarum, et al.
2. Alkaloids: Leonurus japonicus Hoult, Ma Huang, Ricinus communis L., et al.
3. Terpenes and lactones: Tripterygium Wilfordii.
4. Toxic protein: Xanthium, Croton, Abrin, et al.
5. Mineral composition: Cinnabar, Calomel, Mercury, et al.

Manifestation and mechanism of nephrotoxicity associated with TCM

Manifestation: 1. Acute kidney injury: Acute tubular necrosis, allergic/acute interstitial nephritis, rhabdomyolysis, et al; 2. Chronic kidney disease: Chronic interstitial nephritis, renal tubular acidosis, Fanconi's syndrome, urothelial malignancies, nephrolithiasis, obstructive nephropathy, hypokalaemic nephropathy, et al.

Mechanism: 1. Induction of renal cell apoptosis; 2. Oxidative damage; 3. Activation of the relevant immune cells; 4. Inhibition of cell proliferation.

Factors influencing nephrotoxicity associated with TCM

1. TCM aspects: 1) Intrinsic toxicity of herbs; 2) Incorrect botanical identification, incorrect processing, adulteration, lack of standardization of active compounds; 3) Considerable variation in qualitative and quantitative composition; 4) Contamination by heavy metals, mycotoxins, microbial, and pesticides.
2. Treatment aspects: 1) Over dosage, longer than required duration of use; 2) Multi-component and variable mixtures of herbs; 3) Modes of preparation and routes of administration.
3. Patients aspects: 1) Clinical condition (e.g. Chronic Kidney Disease; Allergy); 2) Co-medication (risk of interactions, altered metabolism, additive or synergistic activity); 3) Polymorphism in key metabolic steps according to ethnic or geographical origins.

Prevention of nephrotoxicity associated with TCM

1. Increased attention should be given to the possible nephrotoxicity associated with TCM, to the appropriate preparation, and

also to the co-medication that has already been prescribed to the patient. 2. Preclinical pharmacological and toxicological assessment of TCM is recommended before widespread use, and extreme caution should be observed when using TCM associated with nephrotoxicity. 3. Avoid TCM over-dosage and long-term use. 4. Carefully record all cases of adverse reactions (e.g. renal function, allergy). 5. Develop a much stronger and more stringent system to manage toxicity in TCM.

In conclusion, the use of TM is still relatively common in large parts of the developing world, especially amongst the rural population. The exact incidence of kidney injury due to nephrotoxic TCM has not yet been determined. Further clinical inquiry into the possible use of TCM when investigating a case of unexplained kidney disease should be considered. Regulatory control is also an essential factor in prevention of toxicity due to misuse of TCM.

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LPS-Binding Protein Amplifies TLR-4 Signaling and Pericyte to Myofibroblasts Trans-Differentiation in LPS-Induced Acute Kidney Injury

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Introduction: During sepsis, serum levels of LPS binding protein (LBP) increase and maximize the activation of TLR4-signaling in renal cells, leading to acute kidney injury (AKI). Pericytes (PC) are pivotal in myofibroblasts generation during chronic kidney disease but little is known in AKI. The aim of the present study was to evaluate the occurrence of pericyte to myofibroblast trans-differentiation (PMT) in LPS induced AKI.

Methods: AKI was induced by intravenous LPS infusion in 8 pigs (LPS group). After 3 h from LPS infusion, 8 pigs were treated with coupled plasma filtration adsorption (CPFA). Renal biopsies, performed at 9 h from LPS infusion (T9), were analyzed by IHC and IF. In vitro, PC (PDGFRβ+) were analyzed by FACS, immunofluorescence and western blot. Serum LBP and TGF-beta were quantified by ELISA.

Results: We found the occurrence of acute PMT in LPS-induced AKI, as shown by the reduction of PDGFRβ expression and αSMA increase in peritubular PC. Interestingly, CPFA treatment restored PDGFRβ expression and significantly decreased αSMA⁺PC, in accordance with reduced serum levels of LBP and TGF-beta. In vitro, activation of PC with LPS or endotoxemic sera in vitro led to PMT with Collagen I synthesis and αSMA reorganization in contractile fibers (p < 0.05). The removal of LBP from septic plasma maintained Collagen I and αSMA expression at basal level (p < 0.05). On the contrary, exogenous LBP supplementa-

tion completely reversed CPFA effects. Finally, we found that LPS increased phosphorylation of Smad2/3 and ERK1, respectively ($p < 0.05$) suggesting that acute PMT was induced by both canonical TGF β -Smad2/3 dependent and non-canonical TGF- β -Smad independent signaling (MAPK).

Conclusions: PC might be pivotal in the generation of renal myofibroblasts by PMT during AKI upon the activation of LPS/TLR4 signaling. Selective removal of the LPS adaptor protein LBP may represent a therapeutic option to prevent PC dysfunction and the acute development of renal fibrosis.

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Renal Recovery After Severe AKI in Non-Critical Patients

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Introduction: Acute kidney injury (AKI) is a common event among hospitalized patients, potentially affecting short and long-term clinical outcomes. Understanding the factors associated with renal outcome could be of help in preventing both further acute injury and development of chronic kidney disease (CKD).

Materials and Methods: We performed a retrospective study evaluating patients admitted to Internal Medicine Units of Our Hospital, from 2014 to 2016, who experienced a stage III AKI (KDIGO guidelines), requiring acute hemodialysis treatment (HD).

We included only hemodynamically stable patients, not requiring intensive care. All the patients underwent intermittent HD, scheduled according to the individual need. For each patient we collected history, comorbidity (calculated as Charlson Index-CI), clinical data, laboratory examinations and renal function (evaluated as eGFR, CKD-EPI equation) at the basal control (i.e. last pre-AKI control) and 1, 3, 6 and 12 months after AKI.

Moreover, we also calculated Delta-creatinine as the change of serum creatinine between basal value and AKI onset. Renal recovery was defined as the cessation of HD, while the onset of recovery was defined as the date of the last dialysis treatment.

Results: Thirty-five patients (24 males) with mean age of 70.6 ± 13.8 years we enrolled. Fourteen patients were diabetics, 20 hypertensive; overall basal mean eGFR was of 45.2 ± 26 ml/min with 26 patients (74%) already presenting CKD (i.e. eGFR < 60 mL/min) before the onset of AKI. Causes of AKI were: cardiorenal syndromes (8), drug nephrotoxicity (4), extracellular volume depletion (14), sepsis (6), rhabdomyolysis (1) and acute glomerulonephritis (2).

18 of 35 patients (51%) presented renal recovery after a mean of 16 HD sessions (corresponding to 7.5 ($3.7-17$) days of treatment), while 17 of 35 required maintenance HD treatment and one patient died during the hospital stay.

Patients with renal recovery respect to patients who did not recover were tendentially younger (67.3 ± 13.2 vs. 74.1 ± 13 years, $p = 0.07$), presented a lower CI (5.7 ± 1.9 vs. 7.7 ± 1.9 , $p = 0.005$), high-

er basal eGFR (58.2 ± 7.1 vs. 31.6 ± 16.5 ml/min, $p = 0.002$) and delta-creatinine [IQR, +443 (251–858) vs. +179 (71–330)%, $p = 0.01$]. Interestingly, history of previous AKI episodes was a strong negative predictor of absence of renal recovery (OR 9.0, 95% CI 1.5–51.9, $p = 0.01$). In our small cohort the different causes of AKI did not influence the incidence of renal recovery. The follow-up revealed that eGFR at 3 months was negatively correlated with CI, and directly associated with Delta-creatinine ($r = 0.83$, $p = 0.005$).

Of note, at six-month control 4 of 9 patients (44%) with basal normal renal function presented CKD.

Conclusions: Evaluation of a patient with AKI requires a full consideration of demographic factors, previous clinical history, comorbidities, basal renal function and relative creatinine changes. An episode of AKI, even if occurring in non-critical patients, might represent a risk factor for development of both acute and chronic kidney damage, underlining the necessity to strictly check renal function also in long-term follow-up.

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Multi Organ Failure in a Child with Severe Rhabdomyolysis After Cardiac Transplant Successfully Treated with CRRT with AN69 Heparin Engrafted Filter Oxiris

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Severe low cardiac output after cardiac surgery may often cause multiorgan ischemic failure (MOF) with rhabdomyolysis, inflammatory response and acute kidney injury increasing dramatically mortality rate.

Here we present a case of AKI due to MOF with severe rhabdomyolysis after low cardiac output occurring after heart transplantation in a 14 years-old patient completely recovered with a super high flux CVVHDF with oXiris[®] filter (Gambro, Sweden) (AN69 permanently heparin grafted designed for specific adsorption of endotoxin and cytokines).

A 14 years-old male born with Hypoplastic Right Heart Syndrome treated with Norwood, bidirectional Glenn, Fontan intervention, aortic, cavo-pulmonary connection, multiple caval angioplasty and stent placements during the first 10 years of life, developed progressive worsening of the right cardiac function until protein wasting enteropathy. Various treated until high-protein parenteral nutrition.

In December 2016 he received heart transplantation requiring 100% ECMO placement on day 1. Since day 2 he developed progressive oligo-anuria unresponsive to high dose diuretics, severe hyperkalemia and progressive worsening of cardiac kinetic requiring high dose of amines and worsening of general conditions.

CVVHDF was started while on ECMO through a left femoral vein double-lumen catheter (11 F, 15 cm) at Qb = 180 ml/min, Qd = 5000 ml/h and 1000 ml/h predilution using Prismaflex machine equipped with ST150 filter.

On day 3 Creatine Kinase (CK) and free myoglobin (Myo) dramatically increased showing severe rhabdomyolysis (CK from 1030 UI/L day 1, 150100 UI/L day 2, to 429000 UI/L day 3; Myo from 5000 ng/ml to 18000 ng/ml). The oXiris AN69 filter was therefore placed to optimize the cytokine and cellular degrading products removal and maintained for 96 hours. We observed a rapid decline of CK to 88600 UI/L and Myoglobin to 13725, 14865, 8063 at 24, 48, 72 and 96 hrs respectively and a rapid improvement of hemodynamic stability.

The rapid clearance of rhabdomyolysis and inflammatory cascade products allowed a prompt improvement of the cardiac function and exit from ECMO after 5 days.

CVVHDF progressively was tapered and stopped after 28 days when diuresis and serum creatinine normalized.

This positive experience with this AN69 heparin grafted filter designed to adsorb cytokines, endotoxin and possibly myoglobin should be taken into consideration for severe multiorgan failures with AKI with rhabdomyolysis or septic shock also in children.

Peruzzi Licia is an active SIN member and presenter of the abstract in support of Enrico Cocchi (born on 29/12/1989, age 27).

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Rhabdomyolysis-Associated Acute Kidney Injury in a Patient with Carnitine Palmitoyltransferase II Deficiency

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Introduction: Rhabdomyolysis is a common cause of acute kidney injury (AKI), often secondary to the use of certain drugs (i.e. statins) or to post-traumatic muscular damage. Metabolic conditions, even when involving muscular tissue, rarely result in severe renal damage. Here, we report a case of a patient who experienced AKI and multi-organ failure caused by rhabdomyolysis due to a genetic defect in carnitine palmitoyltransferase II (CPT-II) enzyme.

Case Report: A 66-year-old man presented to the Emergency Department with tremors, dyspnoea, nausea, polyarthralgia and dysuria. Blood pressure on admission was 210/110 mm Hg and blood analysis confirmed a suspected diagnosis of severe rhabdomyolysis (CPK 167,000 mU/mL, AST 3488 mU/mL, ALT 746 mU/mL, LDH 3416 mU/mL) and altered renal function (creatinine 2.28 mg/dL, urea 56 mg/dL). Urine analysis showed haematuria and leukocyturia. After admission, infusive therapy with saline solutions was begun, but in few hours the patient presented a severe worsened of dyspnoea. He was then transferred to the Intensive Care Unit (ICU) where, in light of his rapid deterioration of gas exchanges and hemodynamic instability, the patient was intubated and vasoactive amines were administered. In the meantime, creatinine increased further (5.53 mg/dL) and urine output decreased to the point of anuria, so CRRT was started. Later, CPK serum levels gradually decreased and electromyography showed severe mus-

cle damage, in the absence of signs of acute denervation. A week after the admission into the ICU, respiratory and cardiac conditions improved, while kidney injury persisted. However, in the following days, in concomitance with reduction of CPK levels (87 mU/mL), renal function progressively improved, so that it was possible to withdraw hemodialysis (creatinine 2.04 mg/dL). To explain the cause of the extensive muscle damage, that was conceivably on the basis of pulmonary, cardiac and renal failure, we did a more thorough investigation into the patient's past medical records. Systematic review of past records showed an analogue episode of muscle damage six years before, when after a quadruple CABG surgery for a three-vessel coronary disease, he presented a significant increase in CPK levels (27095 mU/mL), though the aetiology remained unknown. Subsequently, to better define the nature of the muscular damage we tested for myositis that returned negative and a subsequent muscle biopsy revealed primary metabolic myopathy. Biochemical analyses showed an insufficient beta oxidation of fatty acids, with an associated severe carnitine deficit. Ultimately, we proceeded to genetic analysis that finally revealed a diagnosis of CPT II deficiency [homozygosity for c.338C>T (p.S113L)].

Conclusions: CPT-II deficiency is a long-chain fatty acid oxidation deficiency that causes energy depletion in myocytes during prolonged exercise leading to rhabdomyolysis. Clinical manifestations are usually seen in children, but are rarely observed in adults. This case highlights that metabolic alterations should be carefully taken into consideration when evaluating patients with AKI of unclear origin.

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Radioisotopic Evaluation of Glomerular Filtration Rate Before and After Kidney Donation: An Estimation of Renal Functional Reserve (Years 2015–2017)

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Background: After nephrectomy, as a result of the decrease of the nephron mass, kidney donors (KD) develop a partial loss of renal function, defined as AKI (Acute Kidney Injury) according to KDIGO criteria (Clinical Practice Guideline, 2012). The recovery of renal function following AKI is mainly ascribed to the concept of renal reserve function (RFR), defined as the capacity of the kidney to increase glomerular filtration rate. However, there are only few studies on RFR in KD and a correlation with long term functional outcomes.

Aim of the Study: The aim of the present study is to analyze 30 KD renal function before nephrectomy, in the immediate postoperative period and 1 year after the surgical procedure.

Results: KD mean age at the time of donation was 54.4 years (min-max, 30–78), mean serum creatinine 0.73 mg/dL (0.5–0.96), eGFR (CKD-EPI) 99 mL/min/1.73 m² (69–119) and a radioisotope

(⁵¹Cr-EDTA) GFR 101.4 mL/min (78–129). The split function was evaluated by a concomitant scintigraphy using ^{99m}Tc-MAG: the mean percentage of renal function of right kidney was 48% (43–56) and left 52% (44–57), respectively. As expected, immediately after nephrectomy all KD worsened renal function: the mean percentage increase of serum creatinine was 79% (50–112.2%) within 72 hours post-surgery (we observed the peak of creatinine after 24–48 hours in the most of cases); most patients (25/30) developed AKI stage 1, 5 donors stage 2 according to KDIGO criteria. Seven days after surgery, renal recovery was observed in all cases: the mean percentage increase of serum creatinine was 50.6%, significantly lower than the zenit of serum creatinine. These results suggest a potential gain of about 30% in comparison to the starting value of the right kidney. One year after nephrectomy (all left nephrectomies), we studied KD renal function (GFR) using a radioisotopic evaluation of renal function using ⁵¹Cr-EDTA and we then compared it with the split radioisotope (⁵¹Cr-EDTA) GFR of right kidney at the first scintigraphic evaluation. Mean GFR was 68.8 mL/min (50–87) vs. 48.6 mL/min (39.7–60.4) before donation with an average GFR increase of 20 mL/min (0.8–45.6) and a percentage increase of the right renal function up to 110% (mean 42%, min 1.4%).

Conclusions: The results of this study that radioisotopic evaluation is feasible and allows a precise determination of renal function at different time points after nephrectomy in KD. We observed a compensatory hypertrophy in all the 30 KD included in the study independently from age and co-morbidities such as elevated BMI and hypertension, due to the presence of renal functional reserve. This study evaluates RFR only after the decrease of the nephron mass due to donation: we now started a kidney stress test with a protein load to estimate RFR of KD before surgery with the aim of finding a correlation with radioisotopic GFR one year after nephrectomy.

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Great Obese Critically Ill Patient with Acute Kidney Injury and Sepsis

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Introduction: According to a recent multicentre overview AKI manifests in more than half of critically ill patients, and more severe degrees of renal impairment proportionally reduce hospital survival. Here we present the case report of a great obese 47 years old man who underwent hospitalization for acute respiratory insufficiency, acute decompensated heart failure and required renal replacement therapy for the onset of AKI. Because of severely compromised clinical conditions complicated by sepsis and systemic hemodynamic failure, we prescribed a prolonged intermittent renal replacement therapy (PIRRT) combined with hemoperfusion.

Material and Methods: H.A., 47 years old, was admitted at the Emergency Service of our Hospital with severe dyspnea, astenia and obtundation. Physical parameters evidenced very high BMI: 57 (weight: 187 Kg), low blood pressure, arterial blood sample showed hypoxemia and hypercapnia: sO₂ 83.4%, pCO₂ 80.2 mm Hg, pO₂ 47.3 mm Hg, pH 7.12, HCO₃ 19.3 mmol/L. The patient reported progressive decline of urinary output and bladder catheterization confirmed almost absent residual urine. Venous biochemistry demonstrated severe renal insufficiency: creatinine 14.86 mg/dl, azotemia 284 mg/dl, potassium: 6.35 mmol/l. Concomitant diseases were: chronic bronchopneumopathy, chronic heart failure (NYHA class III), dyslipidemia and recent hospitalization (one month before) for acute pancreatitis. The patient was admitted in the Nephrology Unit of our hospital and, given the severely compromised general conditions, he was programmed for a Sustained Low Efficiency Dialysis (SLED) instead of a standard intermittent hemodialysis. A central venous catheter was implanted into the right internal jugular vein and an extemporary urgent cardiological evaluation evidenced a worsened left ventricular ejection fraction, as compared to previous control. The dialytic program was set up as follows: bicarbonate dialysis, with dialysate generated with portable osmosis at a flow rate of 300 ml/min in consideration of the large size of the patient, composed by K⁺ 4 mmol/L, HCO₃ 28 mmol/L, Ca⁺⁺ 1.5 mEq/L. Low flux dialyzer with non polysulfone, syntetic membrane was used (EVAL, KF201, surface area: 1.8 m²). The duration of the treatment was ten hours with ultrafiltration rate of 200 ml/h. Anticoagulation was performed with unfractionated heparin (2000 IU bolus, 800 IU/h in continuous infusion). Blood flow (Qb) was 250 ml/h. Urea distribution volume was 62.3 L.

Results: Worsening hypercapnia, hemodynamic instability and a rapid decline of cognitive status imposed transferring the patient to the Intensive Care Unit (ICU) where he underwent invasive ventilation by means of tracheostomy and continuous infusion of vasoactive amines. The patient was maintained on a Sustained Low Efficiency Daily Dialysis (SLEDD) for persistent anuria and impaired renal function. He well tolerated the treatment without requiring implementation of vasoactive amines. Four days after hospital admission clinical conditions appeared even worsening as fever started, severe anemia required blood transfusions and coagulative factors were progressively consumed. Further biochemical evaluation evidenced positive procalcitonine (19.3 ng/ml), reactive C protein 19.5 mg/dl and significant levels of serum endotoxin (0.74). Hemocultures confirmed sepsis, caused by *Klebsiella oxytoca*. Two consecutive treatments 2 hours daily of hemoperfusion with Toraymyxin device were associated to an Extended Diafiltration with high-flux polysulfone dialyzer, to improve the removal of large inflammatory molecules. After seven prolonged daily dialysis we observed a progressive recovery of urinary output with amelioration of renal function. Hemoperfusion together with aggressive systemic antibiotic therapy guaranteed recovery from sepsis. After more than one month in the ICU the patient was finally readmitted in Nephrology Unit.

Conclusion: Scientific evidence supports the use of long intermittent or continuous dialytic treatments as better suitable in fragile, complicated patients. It is not proved the superiority of continuous renal replacement therapy (CRRT) over PIRRT in term of mortality rate. Here we reported the clinical case of a great obese severely compromised, septic patient in which the use of PIRRT

(SLEDD and Extended Diafiltration, tailored on antropometric features) successfully contributed to the recovery of renal function and was tolerated without further complications for the patient.

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A Case of Acute Kidney Injury: Role of Renal Biopsy in a Puzzling Differential Diagnosis

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A 60-year-old woman with Sjogren syndrome was admitted to another hospital because of chest discomfort, dyspnea, fever and nasal congestion; the first value of creatinine was 0.96 mg/dL. On clinical and instrumental examination bilateral pleural effusion, pericardial effusion, increased blood pressure and atrial fibrillation, which resolved spontaneously, were found. For suspected pericarditis ibuprofen in high doses (600 mg twice a day) was started and the symptoms regressed. The creatinine value was 1.5 mg/dL. Two days after discharge the same syndrome recurred and this time self-administered ibuprofen did not ameliorate the symptoms.

At this point she presented to our hospital; clinical examination confirmed high blood pressure levels and chest radiography showed bilateral pleural effusion only. Echocardiography demonstrated congestive heart failure with a mild pericardial effusion and moderate pulmonary hypertension. For presumed recurrent pericarditis she was started on lysine acetylsalicylate. An elevated creatinine value (2.06 mg/dL) was observed together with a positive urinary sediment, characterized by erythrocytes and granulocytes, granular casts and tubular cells, sometimes forming cellular casts. Proteinuria was in the nephrotic range (7740 mg/24 h).

A rheumatology consultant prescribed methylprednisolone 125 mg/day; she did not improve and developed a hypertensive crisis with acute pulmonary edema, after which she was transferred to the intensive care unit. New onset anemia and thrombocytopenia were noted. The former was associated clinically with esophagitis and reduced levels of haptoglobin, a modest increase in LDH and bilirubin and peripheral schistocytes; the latter was an isolated finding, without evidence of antibodies. Creatinine continued to rise, reaching values of 2.86 mg/dL. ANA and ENA, in particular high Rho levels, were found to be elevated; Scl-70 negative, C3 low and cryoglobulin elevated. In consultation with the rheumatologist, the cardiologist and the hematologist, it was decided to restart methylprednisolone together with mycophenolate mofetil. Moreover, plasmapheresis was performed in the Nephrology ward.

Progressive reduction of creatinine values and improvement in cardiac ejection fraction with a gradual reduction of pericardial and pleural effusions were seen. Proteinuria and positive urinary sediment regressed. Hemoglobin values increased as well as platelet count.

For fever onset, cultures were sent to the laboratory. A urine culture was positive for *K. Pneumoniae*, blood cultures revealed *S. Aureus* and IgM antibodies against Cytomegalovirus were high; therefore antibiotic therapy with cefotaxime and vancomycin and antiviral therapy with ganciclovir were started. The infections cleared.

The complete history of the patient generated a broad differential diagnosis: hemolytic anemia with thrombocytopenia suggested either thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS), but neither neurologic nor gastrointestinal abnormalities were found and antibodies against ADAMTS13 were negative. Serositis, simultaneous renal involvement with an active sediment, hematological abnormalities, concomitant complement consumption and high antibodies levels suggested systemic lupus erythematosus. Another possibility was acute kidney injury in a well-known connectivitis aggravated by non-steroidal drugs with a consequent tubulointerstitial damage. Moreover, an overlap syndrome could not be excluded.

In order to reach a definitive diagnosis the performance of a renal biopsy was pivotal. Light microscopy showed increased mesangial cellularity without increased matrix, and, occasionally, ischemic phenomena with glomerular retraction. Blood cell casts in the tubular lumen were observed. Arteriolar thickening because of intimal hyperplasia with severe restriction of the lumen and a serious obliterating arteriopathy were observed. Immunofluorescence was negative for immunoglobulin, C1q, C3 e C4, κ e λ chains.

The diagnosis was settled: undifferentiated connectivitis with kidney, heart and haematological involvement in known Sjogren syndrome.

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AVF.SIM – Computer Based Surgical Planning of Vascular Access for Hemodialysis

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Background: Arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis (HD), but its creation is still a critical procedure. Our previous activities (FP7-ICT project ARCH) led to the implementation and validation of a patient-specific computational model that reliably predicts the blood flow that occurs inside AVF after maturation for different surgical options, starting from demographic, clinical and imaging (Doppler ultrasounds, DUS) data assessed pre-operatively. We then aimed at translating this computational model in routine clinical practice.

Methods: To allow clinical use of the model we developed a web-based system (AVF.SIM). Demographic and clinical data of patient in need of AVF are collected and US examination is performed to acquire a full upper limb vascular map, including arterial and venous diameters and blood flow in several locations. To simplify collection and transfer, all data are inserted in anony-

mized editable .pdf files and sent to the Coordinating center (Mario Negri Institute) for computer-based simulations. Simulation results are sent to the clinician by email and stored in a secured Document Management System online. About six weeks after surgery a follow-up DUS examination is performed to provide a comparison between measured and predicted AVF blood flow. Data are transferred to the Coordinating center with the same procedure used for pre-operative data.

Results: AVF.SIM allowed to integrate computational modeling of AVF maturation in a single procedure, that includes data collection, data transfer, simulation management and data storing. Simulation results are provided within few hours by the Coordinating center and can provide an additional information to plan AVF surgery. An observational usability test was conducted with 60 patients evaluated by six Italian clinical centers. The accuracy of predicted vs. measured BFV was confirmed to be satisfactory. Regarding the effective usability of the system, this test confirmed AVF.SIM system is easy to use and well accepted in clinical routine, with a limited additional workload for clinicians. The system is currently used by 6 clinical centers, 2 in Europe and 4 in Italy, during routine clinical practice.

Conclusion: Clinical use of AVF.SIM system for surgical planning may help the surgeon to select the best surgical strategy, reducing AVF early failures and complications. This innovative approach allows individualization of AVF care, with the aim of reducing the costs associated with AVF dysfunction and improving the quality of life of ESRD patients.

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Coupled Plasma Filtration and Adsorption (CPFA) for Extracorporeal Detoxification During Acute or Acute on Chronic Liver Failure

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Introduction: CPFA is currently used in the treatment of severe sepsis with the intention of removing the proinflammatory mediators from the systemic circulation. Some evidence exist about the bilirubin adsorbing ability of the neutral styrenic resin which is part of the extracorporeal circuit of CPFA. The aim of this study is to assess efficacy and safety of CPFA in extracorporeal detoxification of liver toxins in patients affected by acute or acute-on-chronic liver failure.

Methods: 9 patients (age 23–61 years) with acute (n = 3) or acute-on-chronic (n = 6) liver failure were enrolled. A total of 22 CPFA treatments were carried out. Each CPFA treatment lasted 6 hours. Unfractionated heparin was used as anticoagulation of the extracorporeal circuit in 7 patients; citrate anticoagulation with the concomitant infusion of calcium chloride in 2 of them. The number of treatment for each patient was established on his/her clinical status. The reduction ratios per session of bilirubin and bile acids were considered. Hemoglobin, platelets, white blood cells, coagulation tests, urea, creatinine, and electrolytes

were also checked on starting CPFA and at the end of CPFA, as biocompatibility measures.

Results: All sessions were well tolerated by the patients. Alcohol was the most common etiology of the liver injury (n = 6), 1 patient was affected by acute cholangitis and Fisher-Evans syndrome, 1 had a viral etiology, and 1 patient had a postoperative jaundice. Median reduction rate per session for total bilirubin was 28% (range 2.2–40); for direct bilirubin was 31.4 (range 8.5–48.6); for indirect bilirubin was 29.1% (range 6.6–65); for bile acids was 30.6% (16.7–59.6); for lactic acid was 30% (range –57.2%–55.6%). In six out of nine patients was observed a recovery of liver function. At one year of follow-up 2 patients died during the hospitalization; 6 patients are followed like outpatients and 1 of them is no more in the waiting list for the transplant; the last one is in course of treatment.

Conclusions: Although CPFA is a non-standardized technique for the liver depuration, its use in patients with acute or acute-on-chronic liver failure has shown favorable effects on safety and efficacy in terms of detoxification. Thus it is considerable a “bridge technique” toward the liver transplant and the recovery of basal liver function.

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Acute Myeloma Kidney: Free Light Chains Removal Associated with Chemotherapy for Patients and Kidney Survival

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Introduction: Renal failure remains a principal cause of morbidity and mortality for patient with multiple myeloma. Among renal manifestation casts nephropathy (Myeloma Kidney) represents the most common. The aim of this study is to assess the efficacy and safety of the extracorporeal removal of free light chains by means of hemodialysis with double filter application in patients with Acute Myeloma Kidney associated with different schemas of chemotherapy.

Methods: Fourteen patients (M/F = 11/ 3) were considered in the study. Acute Myeloma Kidney affected all these patients. Ten patients underwent renal biopsy and 9 cases of myeloma cast nephropathy were diagnosed. The median age of the patients was 70.9 years (range 53–86). Every patient underwent the chemotherapy together with the extracorporeal treatment for the removal of free light chains by using double filter. Hemodialytic treatments were scheduled three times a week and the hemodialysis dose was not related to the degree of the renal failure but to the removal of free light chains. The dialysis filter used were characterized by high adsorptive properties: PMMA filter (polymethylmetacrylate; Filtryzer BK-F 2.1 m² surface area) cut-off 20,000 daltons; PEPA filter (polyester polymer alloy FDX 210-GW, 2.1 m² surface area) cut-off 35,000 daltons. Each dialysis session lasted 4 hours. Low molecular weight heparin was used as anticoagulation. During each session

two dialyzers were used and the substitution of the filter was carried out at the second hour of the hemodialysis session. For each session the reduction rate of free light chains was calculated. Urine output, hemoglobin, platelets, white blood cell, renal function and electrolytes were assessed.

Results: Average number of dialytic session was 10. Median Reduction Rate for free light chains was 25% (range 2.4%–69%). There was no statistical significant difference in FLC reduction rate between PEPA double filter and PMMA double filter (median reduction rate 53% vs. 38%). Six patient involved in the study died because of the complications of multiple myeloma (infections, bone fractures, chronic kidney disease). They all required chronic hemodialysis. Eight patients survived: among these 6 restored their renal function and 2 required chronic hemodialysis treatment.

Discussion: Early removal of free light chains in patient with renal involvement associated with specific chemotherapy is a predictive factor of recovery of renal function and that the recovery of renal function is associated to a best outcome of the patient. The use of an extracorporeal treatment based on substitution of filter at the second hour of the dialytic session was assessed. The two types of filters (PMMA and PEPA) didn't show statistical differences.

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Could Metformin Associated Lactic Acidosis Have a Role in Deposition of Oxalates?

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Introduction: Metformin-associated lactic acidosis (MALA) is a rare complication that can occur in patients affected by diabetes mellitus treated with this biguanide, when associated with simultaneous comorbid conditions as impaired renal function, active alcohol abuse, heart failure, hemodynamic instability, hypoxic states. Its prognosis is severe, with a mortality rate up to 50%.

Case Description: A 65 year old man with a history of benign prostatic hyperplasia and adult onset non insulin dependent diabetes in treatment with metformin, glibenclamide and acarbose, presented to the Emergency Department (ED) for gradual altered mental status and anuria. One week prior to admission the family of patient reported disuria. At admission he was critically ill with impending respiratory failure and hypotension from septic shock due to a urinary tract infection. His arterial blood gas showed metabolic acidosis with elevated serum lactic acid (pH 6.8, pCO₂ 11 mm Hg, pO₂ 147 mm Hg, bicarbonate inestimable, lactic acid 12.7 mmol/l, chloride 100 mmol/l), laboratory tests showed acute kidney injury with serum creatinine until 6.8 mg/dl.

The patient was transferred to intensive care unit and underwent mechanical respiratory support, continuous hemodialysis (CVVHDF), dopamine infusion for persistent hypotension and antibiotic therapy with piperacillin and tazobactam since a urine culture resulted positive for *E. coli*. After eight days of CVVHDF he achieved gradual renal function recovery with high urine output (4 L/die) although serum creatinine was persistently high (6–7.2 mg/dl). After clinical stabilization a renal biopsy was performed. The histological examination showed diffuse deposition of intratubular calcium oxalates with acute tubular necrosis. Abdominal CT showed multiple pancreatic round calcifications compatible with chronic pancreatitis. Fecal elastase resulted <15 microg/g. Therapies included pyridoxine, calcium supplements with a low-fat diet and sufficient potassium citrate to maintain optimal urinary citrate levels. A chronic kidney disease on conservative therapy persisted on discharge of the patient.

Discussion: This case demonstrates that severe clinical condition is the result of multiple processes. First of all the septic status associated with metformin use lead to lactic acidosis. In addition malnutrition caused by pancreatic insufficiency lead to hyperoxaluria caused by increased oxalate absorption; excess free fatty acids in the intestinal lumen bind to calcium allowing absorption in the large bowel of free oxalate. Moreover it could be possible that metformin inhibition of fatty acid oxidation might have a role in deposition of oxalates. It might also be found between a link between severe lactic acidosis and oxalate crystals deposition, since the former condition causes a lowering of urinary pH, and consequently, might produce an environment that induces tubular crystal deposition.