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Can Serum NGAL Levels Be Used as an Inflammation Marker on Hemodialysis Patients with Permanent Catheter?

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Background: Inflammation is a common entity among chronic renal failure (CRF) patients. Neutrophil gelatinase-associated lipocalin (NGAL) is a member of lipocalin family and released from many tissues and cells. We aimed to investigate the relationship between serum NGAL levels and the inflammation markers such as high sensitive CRP (hs-CRP), Interleukin-6 (IL-6) and Tumor Necrosis Factor-Alpha (TNF- α) with different vascular access types used in dialysis patients.

Methods: The study population included 90 patients and 30 healthy age-matched controls. The patients were divided into three groups (I, II, III) and group IV included the controls. In group I and II the patients were with central venous permanent catheter (CVPC) and arterio-venous fistula (AVF) respectively. Group III included 30 patients with CRF. Hemogram, biochemical assays, ferritin, IL-6, hs-CRP, TNF- α and NGAL were evaluated in all groups.

Results: Serum NGAL levels were markedly higher in HD patients with CVPC than in with AVF (7645.80 ± 924.61 vs 4131.20 ± 609.87 pg/ml; $p < 0.05$). Positive correlation were detected between NGAL levels and duration of CVPC ($r = 0.73$, $p = 0.000$), TNF- α ($r = 0.57$, $p = 0.00$), hs-CRP ($r = 0.80$, $p = 0.00$), IL-6 levels ($r = 0.691$, $p = 0.00$) and ferritin ($r = 0.32$, $p = 0.01$), whereas serum NGAL levels were negatively correlated with serum albumin levels ($r = -0.49$, $p = 0.00$). In multiple regression analysis, duration of CVPC, hs-CRP and TNF- α were predictors of serum NGAL in HD patients.

Conclusion: The inflammation was observed in HD patients and increases with CVPC. Our findings show that a strong relationship between serum NGAL levels and inflammation markers. NGAL may be used as a new marker for inflammation in HD patients.

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Education Evolution: A Continuum of Specialist Information Delivery

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Objectives: To review the quality of education delivered to pre-dialysis patients, presenting in either a planned or unplanned way, across one renal unit. To discover if patient choice is consistently offered, with particular focus on peritoneal dialysis (PD) and home haemodialysis (HHD). To determine if PD and HHD information is given accurately. To discover if treatment options education is ever revisited once dialysis therapy has been established.

Methods: Retrospective audit of recorded patient journey through Patient Flow Analysis (PFA). Inclusion criteria based on current patients established on dialysis at the renal unit. Specific factors considered: patient demographics, route to presentation, recorded treatment options education, planned or unplanned start, access type at start, chosen therapy achieved. Treatment choices revisited by specialist nurse, with every established dialysis patient identified. Link nurse network formed and up-skilled in PD and HHD to address ongoing patient education delivery.

Results: The majority of patients did receive timely and accurate treatment options education prior to commencing dialysis. However, a proportion of patients received incomplete or inaccurate information. Some patients didn't receive any home dialysis education at all, regardless of route to therapy. A proportion of patients who chose home did not end up at home. Inconsistencies in education identified, including many perceived barriers to home influencing decision making. HHD was the least discussed. Treatment options rarely revisited once therapy had been established, even when social, health and other patient needs had changed considerably. 273 patients interviewed, 133 (49%) interested in exploring a home therapy further.

Conclusions: Ongoing shared decision making is crucial to maintaining true patient choice. Dialysis is a journey. Over time a patient's needs and experience warrant reassessment of their choice. It is through vigilance to our patients ever changing circumstances that we can be confident that they are being treated with the right modality, in the right place, at the right time.

Acute PD: Unknown, Unplanned, But Not Impossible

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Objectives: Over a six month period, to turn the uncommon practise of acute or unplanned PD (Peritoneal Dialysis) into the everyday. To increase PD penetration by expanding accessibility to acute or unplanned dialysis newcomers. To preserve the modality choice for PD in the event of unplanned circumstances. To adopt a true 'PD 1st' approach by promoting PD as a quality bridge to transplantation, preserving residual renal function and associated early survival advantages whilst simultaneously avoiding the disadvantages of acute central venous catheter use.

Methods: Redesign of the acute / unplanned PD pathway, ensuring continual responsiveness and flexibility to meet dialysis demand. Percutaneous Tenckhoff catheter insertions under local anaesthetic. Redistribution of existing staffing resource to facilitate the pathway. Increasing PD visibility and up skilling staff in the ward environment, addressing any communication gaps. Increased early surveillance to prevent premature modality failure. Early discharge ensured through flexible, individualised, outpatient model of treatment, training and follow up. Utilisation of assisted PD as a training bridge.

Results: Culture change – PD accepted as a viable unplanned modality. PD patient number increased from 81 to 104, PD penetration increased from 14.5% to 17.1%. There were 11 unheralded PD starters during this period, all commencing therapy 0–5 days post catheter insertion (ages ranged from 20–77 yrs). A marked increase in patients with 'perceived' contraindications to PD successfully commencing PD. 1 PD leak which was successfully addressed by reducing fill volumes.

Conclusions: Unheralded presentations continue to make up a large proportion of CKD Stage 5 patients. Supporting this population with acute / unplanned PD is advantageous to both patient experience and PD incident take on. A culture change is required in order to address the perceived barriers to PD. It is in the patient success stories that we can instil confidence in our colleagues and the wider renal community.

The Versatility of Assisted Peritoneal Dialysis (aPD)

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Introduction: Assisted Peritoneal Dialysis (aPD) is an innovative service designed to support patient choice. It enables those who wish to engage with a home dialysis therapy to remain at home, by delivering practical assistance to those who are unable to autonomously maintain their own independent care. The service is delivered by a co-ordinated team of trained Healthcare Assistants (HCA's) who visit the patient's home. The HCA's perform all prescribed practical tasks related to the aPD therapy, carry out basic patient assessment and communicate directly with the referring renal unit. The aim of this work is to retrospectively illustrate the many ways in which aPD can be utilised to improve patient experience.

Methods: aPD commenced as a service in this major London teaching hospital in November 2009. The first patient transferred over from Haemodialysis (HD) due to failed HD access, leaving no other active treatment option available. By year end, two further patients were established on aPD therapy, one as a bridging gap between an unplanned start onto acute PD and training, and the other providing respite for a long-term PD patient experiencing 'burn-out.' In just under 4 years, demand for the aPD service meant expansion to accommodate patients for an even greater variety of needs. From November 2009 to October 2013, 41 patients became a part of the aPD programme at this Unit. These patients have been retrospectively audited, looking at where they came from, why they were selected for aPD, and what the introduction of this modality meant for the patient experience.

Results: 41 patients experienced aPD as a modality during a 48 month period analysed at one renal unit. Reasons for aPD modality selection were wide ranging (Table 1). Of importance, aPD was utilised in 10 cases for unplanned starters on acute intermittent peritoneal dialysis (IPD), and for a variety of reasons including: a bridging therapy until training (allowing for seamless hospital discharge), and short-term assistance until acute symptoms diminished to allow for more successful learning and/or confidence building.

Table 1. Single unit aPD usage for 41 patients over 48 month period (for Abstract 4)

Where did the patients come from?	No. of patients	Reason for aPD
Low Clearance Clinic (LCC)	16	Unable to Self-Care long-term: (16)
Existing PD Patients on Continuous Ambulatory Peritoneal Dialysis (CAPD)	5	Maintain Home Therapy: (5)
Existing PD Patients on Automated Peritoneal Dialysis (APD)	3	Maintain Home Therapy: (3)
Haemodialysis (HD)	5	HD Access failure, no other modality option: (2) Patient choice: (3)
Conservative Care	2	Symptom management: (2)
Unplanned Starters on Intermittent Peritoneal Dialysis (IPD)	10	Short-term bridge to training: (5) Initial assistance / short-term plan: (2) Unable to self-care long term: (3)

Conclusion: Reasons for aPD usage were far ranging and have retrospectively highlighted the essential role of this modality. aPD enables true patient choice for those unable to perform self-care for the long-term, or no longer able to self-care but wishing to remain at home. It provides symptom management for those choosing end of life care, and for patients with loss of HD access and no other alternative therapy, aPD offers the only way to maintain life.

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Successful Term Pregnancy in a Patient with Type 1 Diabetes Mellitus on Long Term Hemodialysis: First in Literature

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Introduction: Pregnancy in patients with end-stage renal disease (ESRD) is rare, and kidney disease before pregnancy is associated with poor fetal outcome. However, the outcome of pregnancy in dialysis patients has been much improved, and the overall rate of successful fetal outcome is reported to be 76%. Maternal diabetes increases the risk of preeclampsia and abnormalities of fetal growth. Type 1 diabetes mellitus (DM) is associated with a three-fold to fivefold increased risk for stillbirth during pregnancy. We present a case of successful pregnancy in a patient with type I DM on hemodialysis (HD).

Case Report: A 34-yr-old primigravida female on hemodialysis for 5 years and type 1 DM for 20 years wanted to get pregnant. Firstly, every kind of risks related with pregnancy, her baby, her life discussed with her and her family. She got fertilized by in vitro fertilization technique in April 2013. She was managed by a multidisciplinary team approach to optimize the patient and fetal outcomes.

At 10 weeks gestation, HD prescription was changed to 4-hr treatments 5 times a week, and a predialysis BUN less than 50 mg/dL was targeted. Throughout pregnancy, predialysis BUN was maintained at 25.1–51.3 mg/dL. Standard unfractionated heparin was used for anticoagulation. Her BP was well controlled with alpha methyl dopa 2x250/day: systolic BP remained at 110–140 mm Hg and diastolic was consistently at 60–80 mm Hg. Anemia was managed with recombinant human erythropoietin and intravenous iron without transfusion. Erythropoietin doses were adjusted to target a maternal Hb between 10–11 g/dL. The median dose was 18,000 IU/week (range, 5,000–26,000 IU/week) during gestational weeks 12–36. In addition, 100 mg intravenous iron sucrose was administered every session during gestational weeks 19–22. The hemoglobin level was maintained above 9.5 g/dL in the third trimester. However, urine volume gradually decreased to less than 100 mL per day.

Fetal growth was appropriate for gestational age. Routine fetal karyotyping was performed at 16 gestational weeks, but mutation screening was not performed. At 35 weeks of gestation, the membrane ruptured during HD, and cesarian section was performed without any complications. She delivered a healthy male weighing 1,900 g. One week after delivery, the patient was hospitalized for 5 days because of postpartum cardiomyopathy.

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Factors Related with Insulin Need in Posttransplant Diabetes

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Introduction: Hyperglycemia that necessitates the use of insulin in patients who were non-diabetic before renal transplantation (renal tx) increases the costs and decreases patient compliance.

Objectives: The aim of this study is to determine the patient and drug related factors that are associated with insulin usage within 3 months and 1 year after renal transplantation.

Methods: We included the non-diabetic renal tx patients who were operated between January 2010 and December 2011. Diagnosis of new onset diabetes after transplantation (NODAT) was made according to American Diabetes Association criteria. Age, gender, body mass index, presence of diabetes in first degree relatives, patients education level, preoperative HbA1c level and immunosuppression were all recorded. We compared the patients that use insulin and non-users at the end of third month and first year after renal tx.

Results: There were 168 patients with NODAT, 3 patients were died during follow-up. At the end of third month, 122 (67.9%) patients were using insulin and in 53 (32.1%) treatment was oral antidiabetics (OAD). After 1 year of posttx, 65 patients (39.4%) were diabetes free, 40 (24.2%) were using insulin and 54 (32.7%) were using OADs. At the end of third month, family history ($p = 0.04$) and education level ($p = 0.03$) was associated with insulin using. Regression analysis for insulin usage at 3rd posttx month was related with diabetes family history ($p = 0.03$, OR = 2.712; 95% CI, 2.131–3.398) and at first year posttx it was related with age ($p = 0.04$, OR = 0.402; 95% CI, 0.184–0.972).

Conclusion: NODAT is related with family history that could be related with multigenic mechanisms in first few months after transplantation. Education level is higher in non-insulin users at third months posttx. That may point the importance of better compliance with diet and treatment. Older patients tend to use insulin at first year posttx which may be related with decreased pancreatic adaptation to glycemic stress.

Plasma Exchange Treatment for Acute Hyperlipidemic Pancreatitis with Falsely Low Levels of Serum Triglycerides – A Case Report

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Hypertriglyceridemia is a well-recognized cause of acute pancreatitis. However, it can produce multiple spurious laboratory results and interfere with diagnosis and treatment of acute pancreatitis. Plasma exchange was shown to rapidly lower the triglyceride level and ameliorate the course of hyperlipidemic acute pancreatitis, but this treatment is not accepted and applied universally.

We present a 55-year-old man who was diagnosed with acute hypertriglyceridemic pancreatitis and transferred to our hospital. At presentation serum triglycerides were severely elevated (104 mmol/l). The repeated laboratory tests showed decreasing serum triglyceride levels (11 mmol/l). However, based on clinical deterioration, increasing levels of serum lipase, worsening respiratory failure and evidently lipemic serum, we decided to perform plasma exchange.

Vascular access was established via right internal jugular vein. During each plasma exchange one estimated plasma volume was exchanged. Two plasma exchange procedures were performed on two consecutive days, procedures lasted 5.6 and 6.6 hours. Plasma was substituted with a solution of 20% human albumin. Anticoagulation was achieved with standard heparin infusion. There were no side-effects of plasma exchange.

Repeated serum laboratory tests obtained before the first plasma exchange procedure revealed that the actual value of serum triglycerides was 57 mmol/l and not 11 mmol/l. After the first plasma exchange procedure serum triglyceride levels decreased to 19 mmol/l. Patient's clinical condition improved dramatically following plasma exchange.

Our report suggests using plasma exchange as early as possible in the course of disease due to its proven effectiveness in the removal of triglycerides. A careful clinical-driven decision making is crucial when treating patients with hypertriglyceridemic acute pancreatitis as the serum triglyceride levels can be falsely low.

Circadian Blood Pressure Behaviour in End Stage Renal Disease Patients Undergoing Haemodialysis. Preliminary Report

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Background: Blood pressure (BP) evaluation and management in patients with end stage renal disease (ESRD) is often a matter of debate. During hemodialysis (HD) hypotension as well as a paradoxical rise in BP may be documented. Intradialytic BP is also variable depending mostly from the weight gain between the HD sessions. We investigated circadian BP behavior in the setting of ESRD.

Methods: We studied 19 patients with ESRD (68% men, mean age 62±19 years, 52% hypertensive) that underwent HD three times a week in the HD unit of our hospital and were at their ideal dry weight. Ambulatory BP monitoring was applied one hour before an HD session and was set to measure BP every 30 minutes and until arrival for the next HD session, for a total of two subsequent 24-hour periods. Blood pressure dipping was defined as [(daytime systolic BP – nighttime systolic BP)/daytime systolic BP]. Patients were defined as dippers if BP dipping was >10% and risers if BP dipping <0%.

Results: Body weight before and after the HD session was 78±28 Kgr and 75±27 mm Hg respectively. Clinic systolic/diastolic BP before the HD session was 133±23/66±11 mm Hg and at the end was 126±25/69±12 mm Hg. Four patients (21%) exhibited intradialytic hypertension defined as a systolic BP increase ≥10 mm Hg from pre- to post HD. Ambulatory systolic/diastolic BP increased not significantly from 127±23/70±13 mm Hg to 130±19/71±11 mm Hg ($p > 0.05$) from the first to the second 24-hour period. Increases were also non-significant for daytime and nighttime BP (128±22 mm Hg vs 129±19 mm Hg and 126±25 mm Hg vs 131±21 mm Hg respectively, $p > 0.05$). Mean dipping was 1.5±7.8% in the first day and further decreased to -0.94±6.8% in the second day. Accordingly, in the first 24-hour period, only 3 patients (16%) were dippers and reduced to 1 patient in the following day (5%). Eight patients (42%) and 9 patients (47%) were risers at the first and second 24-hour period respectively.

Conclusions: Daytime systolic BP does not substantially change during the 48-hour period extending from HD to HD session. Yet, prevalence of the non-dipper as well as the riser pattern is high and further increases during the interdialytic period. Patients with this BP pattern are at high risk for coronary artery disease, especially if other comorbidities coexist. Ambulatory BP monitoring in ESRD patients is a promising non invasive technique for the recognition of future heart disease.

Assessment of Coronary Artery Disease in Patients with End-Stage Renal Disease Using Novel Imaging Techniques

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Background: Coronary artery disease (CAD) is the leading cause of mortality in patients with end-stage renal disease (ESRD). Dobutamine stress echo (DSE) is a well-established non-invasive method for the diagnosis of CAD. The aim of the current study was to evaluate the diagnostic value of DSE in patients with ESRD and its' additive value over rest echocardiographic study using novel imaging techniques.

Methods: Thirty patients with ESRD on dialysis (mean age 61.1±10.4 years old, 21 male) underwent complete transthoracic echocardiographic study (both rest and DSE) and coronary angiography within one month. Left atrial volumes and left ventricular mass index were calculated with the implementation of real-time three-dimensional echocardiography. Wall-motion score index (WMSI) and global longitudinal strain (GLS) were assessed during rest echo study. Dobutamine stress echo was interpreted evaluating the presence of wall motion abnormalities.

Results: Mean duration of dialysis was 78.4 months. Mean ejection fraction was 44.4±11.2%, with mean WMSI 1.35±0.4 and mean GLS was -15.2±4.8%. Mean left atrial volume was 62.8±29.5 ml, while LV mass index was 135±8 g/m². Estimated E/e' ratio was 12.1±2.8. Coronary angiography revealed CAD in 21 patients. Sensitivity and specificity of rest echo was 80% and 64% respectively with cut-off values for WMSI > 1.12, while the respective values for GLS were 85% and 72% (AUC 0.64, cut-off value ≥ -13.5%). On the other hand DSE reported 86% sensitivity and 77% specificity, without statistical significant difference as compared to rest echo study (p = NS).

Conclusion: Complete rest echo study can reveal a variety of abnormal findings. Therefore, dobutamine stress echo, although a sensitive technique, does not seem to offer additive diagnostic value over resting echo study, for the identification of CAD in patients with ESRD. In addition, the implementation of novel imaging techniques as speckle tracking and three-dimensional echo in echocardiographic assessment of such patients seems to be promising.

Plasma Profile in Critical Ill Patients with Cardiorenal Syndrome Type 5

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Background: The Cardiorenal Syndrome Type 5 (CRS5) is defined as a pathophysiology combined dysfunction of heart and kidney due to a wide spectrum of systemic disorders. Sepsis is the most common condition that may cause cardiac and renal dysfunctions. Sepsis is a primary cause of morbidity and mortality in intensive care unit (ICU) patients. Several physiopathogenic mechanisms seem to be involved in CRS5 development. In particular, several cellular and molecular factors such as inflammation, activation of the immune response and activation of apoptotic and necrotic pathways are involved in this syndrome. The aim of the study was examined the plasma profile in CRS5 patients to better understand the mechanisms of this syndrome.

Methods: Twenty-five patients with CRS5 (mean age was 62.8 years ±18.2; men were 19, women were 6) and sixteen healthy volunteers (mean age was 52 years ±7.7; men were 7, women were 9) were recruited for the study. The blood sample was collected on the first day of CRS5 in a EDTA tubes and subsequently centrifuged (3500 rpm for 7 minutes). Plasma was separated from the blood cell and stored at -80°C until use. Control samples were processed in the same manners.

Quantitative determination of IL-6, TNF-α, IFN-γ and IL-18 was performed by Human Instant Enzyme-Linked Immuno-Sorbent Assay (ELISA) kit (eBioscience) in plasma. The amount of these molecules (pg/ml) were calculated from the standard curves according to manufactures protocol and instructions. Optical density was read by using a VictorX4 Multilabel Plate Reader (PerkinElmer Life Sciences) at 450 nm. All test were performed in triplicate. Quantitative analysis of Neutrophil Gelatinase-Associated Lipocalin (NGAL) and B-type natriuretic peptide (BNP) in plasma EDTA was performed by ALERE TRIAGE assay by Cardiorenal Panel (Alere). Statistical analysis was performed using the SPSS 15 Software package. A p-value of <0.05 was considered statistically significant.

Results: 44% of CRS5 patients required renal replacement therapy (RRT). 33% of these patients had negative outcome during ICU stay. BNP and NGAL levels were significantly higher in patients with CRS5 [BNP: 888.5 pg/ml, (IQR: 523.3–2244.3); NGAL: 1300 ng/ml, (IQR: 1300–502)], these levels indicated heart and kidney combined dysfunction and damage.

Furthermore, IL-6 and IL-18 levels were significantly higher in CRS5 patients compared with healthy controls (p < 0.01). Quantitative analysis of TNF-α and IFN-γ levels are similar in CRS5 patients and healthy controls.

Conclusions: Our study suggests that proinflammatory response likely contributes to distant organ dysfunctions in CRS5 patients. The bidirectional cross-talk between kidneys and heart in Cardiorenal Syndrome may contribute to the poor outcome in these critical ill patients.

Cardiorenal Syndrome Type 5: A New Mechanism for Heart-Kidney Crosstalk

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Background: In Cardiorenal Syndrome Type 5 (CRS type 5), heart and kidney are both targets of a strong systemic inflammatory reactions. It reflects concomitant cardiac and renal dysfunction in the setting of a wide spectrum of systemic disorders, like Sepsis, Diabete Mellitus and Systemic Lupus Erythematosus. In CRS type 5, cardiac and renal dysfunctions are often observed. AKI is a common complication in septic patients and carries poor prognosis. CRS type 5 is characterized by generalized inflammatory response and activation of coagulation and fibrinolytic system. In critical ill patients inflammation, abnormal cell signaling, cell cycle arrest, mitochondria dysfunction were observed and can induce direct pro-apoptotic and pro-inflammatory effect on cardiomyocytes and kidney cells (podocytes, endothelial cells, mesangial cells and tubular epithelial cells). CRS type 5 mechanism is not well-known, although specific cellular and molecular changes with time-specific pattern are reported. Our aim was to examine in vitro that CRS type 5 plasma was able to trigger a response in renal tubular cells (RTC), resulting in apoptosis and cytokine-release.

Methods: We enrolled 11 patients with CRS 5 (age 68.4±10.8 years) and 16 controls (CTR) (age 52.0±7.7 years). Blood samples were collected in EDTA tubes and subsequently centrifuged 7 minutes at 3500 rpm. Plasma was immediately separated from blood red cells and stored at -80°C until use. Plasma from different groups were incubated with Renal Tubular Cells (RTC) for 24 h and, subsequently, cell apoptosis, necrosis and viability were evaluated by Annexin-V/Propidium Iodide assay using flow cytometer (Navios, Beckman Coulter). Plasma levels of IL-6 were detected by Human Instant enzyme-linked immune-sorbent assay (ELISA) test (eBioscience). The amount of IL-6 (pg/ml) was calculated from the standard curve according to the manufacturer's protocol. All test were performed in duplicated. Statistical analysis was performed using STATA software. A *p*-value of <0.05 was considered statistically significant.

Result: The RTCs incubated with plasma from CRS type 5 patients showed significantly higher apoptosis and necrosis rates (*p* < 0.001) compared with those incubated with plasma from healthy subjects. A significantly lower viability was observed in RTCs incubated with CRS type 5 plasma compared to controls (*p* < 0.001). In CRS type 5 plasma, IL-6 levels (64.6 pg/ml, IQR 59.1–96.3) were significantly higher compared with controls plasma (6.17 pg/ml, IQR 3.50–7.78) (*p* < 0.001). Moreover, there were significant positive correlation between IL-6 and cellular apoptosis ($\rho = 0.74$, *p* < 0.001) and necrosis ($\rho = 0.56$, *p* < 0.01). Instead, a negative correlation ($\rho = -0.74$, *p* < 0.001) was observed between IL-6 levels and viability.

Conclusions: Our study demonstrated the induction of apoptosis and necrosis pathways in RTCs incubated with CRS type 5 plasma. Furthermore, we observed an increase of IL-6 plasma levels in CRS type 5 patients and a positive correlation between this cytokine and cellular apoptosis. In conclusion we can hypothesize that IL-6 could trigger apoptosis in renal tubular cells. Moreover, we could theorize a possible implication of inflammatory damage on the pathophysiology of CRS type 5.

Survey of Acute Kidney Injury and Related Risk Factors of Mortality in Hospitalized Patients

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Conflicts of Interest: None of the authors have any conflict of interest to declare.

Objective: The main aim of this study is to investigate the incidence and prognosis of acute kidney injury (AKI) and to clarify the risk factors associated with the prognosis of AKI in hospitalized patients.

Method: All patients hospitalized from Jan 1st. to Dec 31th. 2012 in Ren Ji Hospital, School of Medicine Shanghai Jiao Tong University were screened by the Lab Administration Network. All the patients with intact medical history of AKI according to the Acute Kidney Injury Network (AKIN) were enrolled in the study cohort. AKI's incidence and etiology, as well as the patient's characteristics and prognosis, were retrospectively analyzed. Logistic regression analysis was used to investigate the risk factors on the patient prognosis and renal outcome.

Results: 934 AKI patients were enrolled. The incidence of AKI in hospitalized patients was 2.41%. The ratio of males to females of patients was 1.88:1 and the mean age was 60.82±16.94 years. The incidence of AKI increased with the increasing of age. Among hospitalized patients, 63.4% were from the surgical department, 35.4% from the internal medicine department and 1.2% from the obstetric and gynecologic department. Regarding the cause of AKI, pre-renal AKI, acute tubular necrosis (ATN), acute glomerulonephritis and vasculitis (AGV), acute interstitial nephritis (AIN) and post-renal AKI were contributed to 51.7%, 37.7%, 3.8%, 3.5% and

3.3% respectively. The survival rate on the day 28 after AKI was 71.8%. In addition, 65.7% patients got complete renal recovery while 16.9% got partial renal recovery and 17.4% got renal loss. The mortality of AKI in hospitalized patients at Stage I, Stage II and Stage III were 24.8%, 31.2% and 43.7% respectively. Multivariate Logistic regression analysis showed that use of nephrotoxic drugs, [Odds Ratio (OR) = 2.313], hypotension in the previous week (OR = 4.482), oliguria (OR = 5.267), the number of extra-renal organ failure (OR = 1.376) and renal replacement therapy (RRT) (OR = 4.221) were independent risk factors for mortality. The number of extra-renal organ failure (OR = 1.529) and RRT (OR = 2.117) were independent risk factors for renal loss.

Conclusion: AKI is one of the most common complications in hospitalized patients. The mortality is high and renal prognosis is poor after AKI. The prognosis is closely associated with the severity of AKI. Nephrotoxic drugs, hypotension within the last week, oliguria, the number of extra-renal organ failure and RRT are independent risk factors for patient death; while the number of extra-renal organ failure and RRT are independent risk factors for renal loss.

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Oxidative Stress: The Role in the Pathogenesis of Cardiorenal Syndrome Type 1

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Background: Cardiorenal syndrome (CRS) Type 1 is characterized by a rapid worsening of cardiac function leading to acute kidney injury (AKI). CRS Type 1 pathophysiology is complex and unclear as it involves several interrelated factors. It is postulated that the concurrent dysfunction of heart and kidneys is due to a cellular and molecular crosstalk between these organs. Key physical, chemical and biological processes may be involved. Furthermore, an immune-mediated damage, an alterations in the immune response with apoptosis, cytokine-release and changes in immune cell functions, have been hypothesized as a potential mechanisms involved in the pathogenesis of CRS. Loss of redox homeostasis in reactive oxygen species (ROS) and reactive nitrogen species (RNS) results in a proinflammatory and profibrotic milieu via distinct mechanisms which promotes cardiovascular and renal structural and functional abnormalities.

In this pilot study, we examined the putative role of ROS/RNS-linked oxidative stress as a pathogenic mechanism of Cardiorenal Syndrome Type 1.

Methods: Subjects were selected from a prospective community-based cohort study with Acute Heart Failure (HF) (58% male, mean age 80±8 years, median Crea 0.98 mg/dl, IQR 0.87–1.15), CRS1 (54% male, mean age 76±10 years, median Crea 1.34 mg/dl, IQR 1.12–1.83). Patients who had AKI prior to the episode of AHF, or had any other potential causes of AKI, were excluded from the

study. We included patients with acute heart failure without AKI in the study to better analyze the contribution of HF to oxidative stress. Quantitative determinations for Interleukin-6 (IL-6), Myeloperoxidase (MPO), Nitric Oxide (NO), Copper/Zinc Superoxide Dismutase (Cu/ZnSOD), and Endogenous Peroxidase Activity (EPA) were performed in HF (n = 12), and CRS1 (n = 11) patients. The amount of IL-6 (pg/ml), MPO (pg/ml), NO (μM), Cu/ZnSOD (pg/ml) (ng/ml) and EPA (U/l) were calculated from the standard curves according to the manufacturer's protocol.

A *p*-value of <0.05 was considered statistically significant. All statistical tests were performed with SPSS.

Results: CRS1 patients displayed significant augmentation in circulating ROS and RNS, as well as expression of inflammatory cytokines, as IL-6 (*p* < 0.05).

Quantitative analysis of all oxidative stress markers showed significantly lower oxidative stress levels in HF compared to CRS1 patients (*p* < 0.05).

This pilot study demonstrates the significantly heightened presence of dual redox disequilibrium in CRS1 compared to HF patients: ROS/RNS production involving NADPH oxidase and MPO; superoxide production of hydrogen peroxide and NO; up-regulation of proinflammatory mediators via peroxynitrite.

Conclusion: For the first time we demonstrate evidence for the delineation of 2 distinct oxidative roles in CRS1 pathogenesis. Our findings indicate that oxidative stress is a potential therapeutic target, as it promotes inflammation by ROS/RNS-linked pathogenesis.

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Cell-Free Plasma DNA in Peritonitis Is Originated from Apoptotic Events

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Peritonitis are a common and serious complication of peritoneal dialysis (PD) and a frequent cause of technique discontinuation. Cell-free plasma DNA (cfpDNA) is a circulating extracellular DNA fragments which originates from necrotic and apoptotic cells derived from inflammatory events and tissue damage. High levels of cfpDNA have been reported in many clinical conditions. In particular, cfpDNA is increased in PD patients plasma with a recent episode of peritonitis. Our aims were:

- to confirm the variation in plasma levels of cfpDNA after an episode of peritonitis in chronic PD patients;
- to elucidate the putative causative mechanism involved in cfpDNA formation during peritonitis.

We enrolled 54 PD patients undergoing maintenance PD for a minimum of 3 months and we divided them into 3 different groups: 25 PD patients without any history of peritonitis, 21 PD patients whose last episode of peritonitis was more than 3 months

Fig. 1. (for Abstract 14).

Fig. 2. (for Abstract 14).

prior to enrollment, and 8 patients who had an episode of peritonitis within the 3 months prior to enrollment.

CfpDNA was extracted from plasma and was quantified by Real time PCR for the β -globin gene, in triplicate. Subsequent, qualitative analysis of apoptosis was performed by DNA Ladder kit and quantitative plasma levels of Caspase-3 was measured by ELISA test (eBioscience).

Quantitative analysis of cfpDNA showed significantly higher levels in patients who had an episode of peritonitis within the 3 months compared with patients without peritonitis and without peritonitis in the last 3 months ($p < 0.01$) (figure 1). Qualitative analysis of apoptosis showed higher DNA ladder formations, suggesting presence of apoptotic events. Caspase-3 activation proved the increase of apoptotic events ($p < 0.01$) and a significant correlation was observed between cfpDNA and Caspase-3 levels (figure 2). Lower levels of cfpDNA and Caspase-3 were observed in pa-

tients with a longer peritonitis-free period. cfpDNA levels tend to progressively decrease in correlation with peritonitis-free time.

In conclusion, our data has demonstrated that cfpDNA is increased in the plasma of PD patients with recent peritonitis. We hypothesize that cell apoptosis induced by Caspase-3 activation is one of the potential sources of cfpDNA.

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Liver-Kidney Crosstalk: From Physiological to Pathological Relationship

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The 'organ crosstalk' can define as the complex biological communication, signaling and feedback between distant organs mediated via cellular, molecular, neural, endocrine and paracrine factors. This interaction underlines that one malfunctioning and damaged organ can induce structural and functional dysfunction in distant organs.

Liver and kidney are important regulators of body homeostasis and are involved in excreting the toxic by-production of metabolism and exogenous drugs.

The pathogenesis of liver-kidney crosstalk is poorly understood, largely because of the low number of relevant experimental studies; a better understanding of the pathophysiology of this bidirectional crosstalk may offer improved management strategies.

Liver-kidney crosstalk likely occurs by a complex combination of soluble inflammatory mediators and cellular immunity. Pro-inflammatory cytokines, reactive oxygen species (ROS) and he-

patic/renal apoptosis may play an important role in renal-liver injury. Non resolving and persistent exposure to pro-inflammatory factors, such as TNF- α , IL-1 β , IL-4, IL-6, IL-13, IL-17, leads to tissue damage, liver and kidney dysfunction and failure. Loss of homeostasis in ROS and reactive nitrogen species (RNS) during liver-kidney crosstalk results in an immune system activation and in a pro-inflammatory and pro-fibrotic milieu via distinct mechanisms which stimulate structural and functional abnormalities implicated in regulation of apoptosis and in the regeneration of hepatocytes.

An important mechanism of end-organ dysfunction in liver-kidney crosstalk is the development of renal failure: dysregulation of vasoactive mediators leads to acute kidney dysfunction and systemic volume overload is increased causing liver failure.

Inflammatory processes, oxidative stress, apoptosis activation and small RNA regulation are likely key components in liver-kidney crosstalk. Rapid characterization of cellular, subcellular and molecular research in human and animal models continues to elucidate the complex crosstalk as well as putative epigenetic changes resulting from brief or chronic states of immune-inflammatory changes in gene expression. Moreover, the combination of genomics, transcriptomics and proteomics researches has moved towards systems biology which offers the opportunity for a global comprehension of organ crosstalk and human disease. Present and future studies on pathogenetic mechanisms involved in liver-kidney crosstalk will allow the development not only of better directed but also of more appropriately timed therapeutic strategies to improve outcome in these patients.

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Assessment of Cardiovascular Risk in Patients on Chronic Hemodialysis Using Pulse Wave Velocity (PWV)

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Introduction: Cardiovascular disease (CVD) is common in end-stage renal disease (ESRD) patients and considered to be one of the most common causes of death. Widespread atherosclerosis is common in patients with ESRD. Ultrasonographic measurement of pulse wave velocity (PWV) is utilized to detect the arterial stiffness that is associated with various cardiovascular diseases.

Objectives: To investigate the vascular calcification in ESRD patients on regular hemodialysis by using PWV and to establish the relationship between the PWV results with different laboratory parameter and regular medications.

Patients and Methods: Twenty patients treated with regular hemodialysis (13 males and 7 females with mean age 68.9 ± 15.2 years). All study participants underwent Carotid-Femoral PWV which was measured by using a SphygmoCor device and laboratory parameters related to cardiovascular risk were prospectively assessed. All those measurements have been performed after termination of the dialysis session.

Results: Average normal value for PWV was 10.3 m/s (5.5–15). 8 patients (40%) [6 males and 2 females] showed higher PWV values.

PWV showed statistically significant correlation with serum phosphorus (PO_4) ($P = 0.0129$), calcium supplements ($P = 0.0236$) and a trend towards a positive correlation with Serum low-density lipoprotein (LDL) ($P = 0.0681$).

On the multivariable linear regression analysis showed that the association for the calcium supplement was largely explained by the S.Po_4 , and the variable really associated with PWV was S.Po_4 ($P = 0.0242$). No statistically significant correlation between PWV and Serum Calcium, PTH and Vitamin-D ($P = 0.2423$, 0.4722 and 0.5128 respectively). Also there was no significant correlation between the PWV and Vitamin-D supplementation [15 patients received it (mean 9.4 & $P = 0.9328$)]. This could be related to low number of the study population, which could be expanded in later stage of the study.

Conclusions: Patients on regular hemodialysis are already susceptible to atherosclerosis and cardiovascular complications. Carotid-Femoral PWV scores provide independent predictive information for the occurrence of cardiovascular events and mortality in hemodialysis patients and help to identify high risk patients. These measures characterized by being non-invasive, inexpensive, easily and rapidly performed and widely available which make them applicable candidates for the daily clinical practice which in turn will be reflected into a survival benefits.

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Influence of Haemodialysis on the Variations of Serum Levels of 25 Hydroxyvitamin D

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Introduction: The management of nutritional supplements of vitamin D in patients on haemodialysis (HD) remains a very controversial practice. There is controversy about which type of vitamin D to supplement, how to do that and in which dose. These treatments are influenced by multiple factors such as sun exposure, body fat and other co-administered treatment. We do not know the influence of HD on the levels of 25 OH vitamin D (25OHD).

Objectives:

- Determine the evolution in time of serum 25OHD values after administration of 16,000 U of 25OHD3.
- Observe the influence of HD on the variations of the 25OHD levels.

Materials and Methods: In 17 stable HD patients (11 women and 6 men, mean age 71 ± 14), an oral ampoule of 25OHD3 16000 units was administered during the winter. Baseline and pre-dialysis 25OHD determinations were performed for 2 weeks. In addition, 11 patients post dialysis 25OHD determinations were performed for 2 weeks. None of the patients administered any other metabolite of vitamin D or selective activator.

Results: The mean baseline 25-OH-D was 17.40 ± 8.62 ng/ml. In the next session levels were 16.62 ± 6.96 ng/ml (ns). There was

great variability between patients. However, in 8 of 17 patients (47.1%) the levels increased more than 10%. The preHD levels decreased slowly in the following 5 sessions: 15.28 ± 7.54 , 15.22 ± 7.01 , 14.73 ± 8.26 , 14.91 ± 7.76 and 14.77 ± 9.19 . By comparing these values and the variation of those of the baseline by ANOVA for the repeated measures, it appears that there is no relationship between taking the ampoule and subsequent vitamin D levels (non significant), however this could be explained by a large dispersion of values. By plotting the variation in 25OHD levels from baseline it showed a trend. To try to estimate a linear trend adjusted linear regression model for repeated measures or mixed effects model. The coefficient of linear trend was -0.0283 , which means that each determination decreases 3% from baseline ($p = 0.0249$).

In addition, 11 patients' post-dialysis 25OHD controls were obtained. We observed no significant differences between the values of 25OHD pre and post-dialysis, HD1 pre: 16.37 ± 7.50 post: 15.85 ± 9.72 , HD2 pre: 15.36 ± 8.05 post: 16.00 ± 8.9 , HD3 pre: 15.09 ± 7.68 post: 15.4 ± 7.78 , HD4 pre: 15.22 ± 9.74 post: 14.65 ± 9.3 , HD5 pre: 14.58 ± 10.16 16.19 ± 8.28 post (ns).

Conclusion:

1. There is great individual variability in the increase in serum 25OHD after oral administration of 16,000 U of 25OHD3 and in winter this study, an overall significant increase was observed.
2. In 2 weeks, 25OHD levels decreased slowly down to the baseline levels but have not been modified by the HD session.

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Therapeutic Response of the 25 Hydroxyvitamin D Levels After Administration of Calcidiol in Patients on Regular Hemodialysis

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Introduction: According to the recommendations of the Spanish Society of Nephrology, the values of 25OHD should be maintained >30 ng/ml. There is controversy about what is the best guideline for clinical practice. The most commonly used in Spain is Calcidiol supplementation, although other groups advise the use of cholecalciferol to avoid adverse effects such as hypercalcemia. However, there are a lot of factors that can alter the effectiveness or induce toxicity of the treatment.

Objectives:

- a) Observe the 25OHD levels after administration of 16000 units Calcidiol in patients on haemodialysis (HD) patients.
- b) Determine whether treatment with Calcidiol affects the serum concentrations of Calcium (Ca), Phosphorus (P) and PTH.
- c) Determine whether FGF23 affect baseline calcidiol response.

Materials and Methods: 27 HD patients (10 males, 17 females and mean age of 72.3 ± 13.58 years) were administered 1 ampoule of 16000 units of Calcidiol (Hidroferol®) at the first HD session of the week (HDb). Measurement of the serum levels of 25OHD, Ca, P and PTH have been performed before administration and before the following dialysis sessions for a week (HD1, HD2,

HD3). Also measurement of the FGF23 baseline has been performed.

Results:

- The 25OHD was: HDb: 16.49 ± 7.29 ng/dl, HD1: 18.68 ± 7.5 and HD3: 16.07 ± 6.71 (ns). Only 59% of the patients showed increased level of 25OHD levels $>10\%$, while no change has been detected in the rest of the patients.
- The Ca was 9.15 ± 0.69 , Ca1 = 8.8 ± 0.56 and Ca3 = 8.6 ± 0.63 , with 4% decrease from the basal calcium levels ($p = 0.0001$). The percentage of patients who had Ca >9.5 was HDb = 22.2%, HD1 = 12%, HD3 = 14.8%.
- The P was 3.66 ± 1.55 , P1 = 4.36 ± 1.73 and P3 = 4.34 ± 1.92 , with 36% increase from the basal level ($p = 0.0047$). The percentage of patients with P > 4.5 was HDb = 22.2%, HD1 = 44%, HD3 = 40.7%.
- PTH levels were not changed; PTHb = 417.19 ± 572.95 , PTH1 = 448.41 ± 497.23 , PTH3 = 449.05 ± 474.64 (ns).
- The FGF23b was 3292.59 ± 5101.32 . In patients with increased 25OHD1 $>10\%$, FGF23b was 2375 ± 3550 , while in those with 25OHD1 increased $<10\%$: FGF23 was 5127 ± 6619.77 (n.s).

Conclusions:

- 1) There was a high heterogeneity in 25OHD levels after Calcidiol supplementation.
- 2) Statistical significant differences ($p < 0.05$) were found between baseline and 48 hours of serum Calcium and phosphorus after Calcidiol treatment with reduction of calcium and increase of phosphorus levels.
- 3) No changes have been detected in PTH levels over one week.
- 4) A trend to a better response to supplementation with higher levels of FGF23 was shown that has been explored in larger series and could be attributed to a lower conversion to 1,25 (OH) VitD.
- 5) The basal FGF23 values didn't show significant response to Calcidiol, although there was a trend to better response to supplementation with lower levels of FGF23.

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Pumps in Wearable Artificial Kidneys

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The Wearable Artificial Kidney (WAK) is a device that allows prolonged and frequent dialysis treatments for patients with End Stage Renal Disease (ESRD), providing a practical and feasible solution to satisfy the need for a continuous dialysis, since it is supposed to operate like a real kidney.

The WAK consists of a battery, an external flowmeter, a dialyzer and three basic systems: one for regenerating the dialysate, an alarm/shutoff one and a pumping one. A pump is defined as a device which moves fluids by mechanical action; in the case of

WAK, the pumping system is responsible for propelling blood and dialysate through the tubing of extracorporeal circuits. Thus, many of the WAK's most important characteristics, such as its flow rate, are strictly related to its pumping system.

Many different pumps' designs have been suggested for WAK. In the actual prototype, the pumping system is mainly constituted by blood and infusion pumps.

Blood pumps can be distinguished, according to the way they work, in positive displacement, peristaltic, dynamic, kinetic centrifugal, turbine, shuttle and rotary pumps. They all, depending on the category they belong, are characterized by different values of the most important parameters defining their quality: safety, biocompatibility, MTBF (Mean Time Between Failures), flow rate, hemolysis and cost.

Thus, an 'ideal' pump, in such a context, would be highly safe, very ergonomic and both accurate and precise, as well as biocompatible, with an infinite MTBF, and with smooth shaped mean valued flux speeds.

On the other hand, whether its energy consumption, or its weight, size and cost should be as low as possible, together with the hemolysis it produces which would bottom out.

The main aim of this article is to analyze in detail the WAK pumping system.

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Pauci-Immune Crescentic Glomerulonephritis Secondary to Vasculitis P-ANCA

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Pauci-immune crescentic glomerulonephritis usually is a component of a systemic small vessel vasculitis, however some patients have renal-limited involvement. They are characterized by little or no deposition of immune complexes in the vessel wall and the use of immunosuppressive agents has dramatically improved the short and long-term outcomes of ANCA vasculitis with systemic disease.

Woman of 68 year-old, with hypothyroidism treated in the past with propylthiouracil and dislipidemia. Normal renal function in February 2013, with serum creatinine of 0.6 mg/dL. In March of the same year started with symptoms of dyspnea, cough with sputum, hemoptysis and fever (38°C) since three weeks, without recovery to levofloxacin treatment. Laboratory findings established anemia (Hb: 7.3 g/dL), leukocytosis (16400/uL), thrombocytosis (503000/uL), urea: 120 mg/dL, creatinine: 3.0 mg/dL and C-reactive protein: 19.5 mg/dL. Urinalysis included hematuria (30–35 red cells per high-power field) and proteinuria in a sub-nephrotic range (1 g/day) at 24h-urine collection. Immunologic study showed positivity to ANCA (anti-MPO): 59.0, normal complement component and virology was negative. Endoscopy revealed a nodular region of duodenum, without signs of malignancy on histology. She was submitted to *fluid challenge* and blood transfusion (3 units) without any improvement. Thoracic tomography exhibited bilateral alveolar infiltrates. For the suspi-

cion of sistemic vasculitis, we started pulses of methylprednisolone (1 g for 3 days) followed by oral prednisolone (1 mg/Kg/day) with very good response. Renal biopsy proved crescents in half of the 16 glomeruli and 50% of cortical fibrosis and tubular atrophy. Immunofluorescence microscopy revealed little linear deposits of IgG, sustained the diagnosis of glomerulonephritis pauci-immune and crescentic.

The interest of this case is to demonstrate the dramatic improvement with normalization of renal function and resolution of respiratory symptoms just with corticosteroid treatment. The addition of cyclophosphamide was not performed because of favorable evolution and for the suspicion of gastric cancer.

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Renal Replacement Therapies in Acute Decompensated Heart Failure Admissions. The Real World. Experience in a Single Center

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Aims: Patients (P) hospitalized for acute heart failure (AHF) syndromes may receive renal replacement therapy (RRT) during hospital course. This population has not been well characterized. We aimed to describe a cohort of P who received RRT during hospitalization as part of AHF treatment.

Methods: Demographic and clinical data were recorded. P were divided into 3 groups: group 1) permanent RRT after AHF hospitalization; group 2) transient RRT during hospital stay; group 3) Chronic kidney disease V (CKD V) under chronic dialysis support. Length of stay (LOS), mortality and readmission rates at 150 days are showed.

Results: A total of 48 consecutive P were admitted between July 2009 and March 2014. 66% were males aged 67 ± 14 years old (NSS among groups). Blood pressure at admission was $129 \pm 36/76 \pm 18$ mm Hg and heart rate 93 ± 22 bpm. 64% of P had previous arterial hypertension; 10% atrial fibrillation and 25% were diabetics. Previous Chronic kidney disease was found in 79%; while 19% were on chronic dialysis at admission and 39% at hospital discharge 39%. The distribution of P in the differents groups was 22.91% in group 1; 58.33% in group 2 and 18.75% of P in group 3.

Prior to admission 64% of P had class II and 28% of P class III of NYHA classification 60% had left Systolic dysfunction. Left ventricular ejection fraction was $43 \pm 15\%$. Severe aortic or mitral valve disease was found in 28.6%. Inotropic support was needed in 35%. 60% P had hospitalization longer than 7 days. 60% of all P were previously hospitalized for AHF.

In group 2 Prolonged LOS (>7 days) was more prevalent: 72% vs 42%; $p = 0.03$; OR 3.6; 95%CI (1.06–12), and the mortality was higher (mainly due to in-hospital death): 87 vs 33%; $p < 0.001$; OR 14; 95%CI (3.2–61) than in all P. The group 3 had shorter LOS (5% vs 21%; $p = 0.01$). Time to first readmission was longer in group 1 (13 d vs 95 d; $p = 0.02$).

Conclusions: AHF patients who need transient RRT during hospitalization (group 2) define a high risk group for death or re-admission. Chronic dialysis Patients hospitalized for AHF symptoms are at lower risk for cardiac events.

Me parece que habría que poner los datos de cada grupo en mortalidad y tiempo de hospitalización, además de dejar lo que se marcó como significativo.

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Acute Kidney Injury and the Brain

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Acute kidney injury (AKI) should never be conceived as a single, independent pathology, but as an event that can be either be a result of or a trigger to a multiorgan dysfunction, that may arise from any organ injury, and perpetuates the organ dysfunction cascade through complex biohumoral pathways, ultimately leading to Multiple Organ failure (MOF) and death. Recent evidences suggest that AKI diagnosis should be considered even before filtration function loss occurs by using tubular damage biomarkers, ('sub-clinical' Acute kidney Injury, SAKI).

Current literature on experimental studies revealed multiple pathways and mechanisms of kidney injury in AKI: local activation of the coagulation system, infiltration by leukocytes, endothelial injury, expression of adhesion molecules, release of cytokines, induction of toll-like receptors, activation of intra-renal vasoconstrictor pathways, induction of apoptosis, changes in tubular cells with loss or inversion of polarity and loss of adhesion to the basement membrane.

The general global mechanism involved in distant organ injury in AKI may be described as: Cytokines/chemokines induced damage, leukocyte extravasation, oxidative-stress and dysregulation of sodium and water channels. This mechanisms give place to venous congestion, altered vascular permeability, apoptosis and necrosis, leading to organ dysfunction that propagates itself up to MOF and death.

The forementioned basic mechanism has also been described related to the brain damage associated to AKI: renal ischemia reperfusion was found to result in increased neuronal pyknosis and microgliosis in the hippocampus, increased brain vascular permeability, microvascular protein leakage, and disruption of the blood-brain barrier. In has also been described a decreased dopamine turnover in the striatum, mesencephalon, and hypothalamus 48 hours after bilateral renal ischemia reperfusion.

The main aim of this article is to review the current literature on the AKI effects on the brain.

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The PAKI (Pediatric Acute Kidney Injury) Registry

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Background: Advancements and improvements in care for critically ill pediatric population has led to fast changes in pediatric acute kidney injury AKI epidemiology. Prevalent causes leading to pediatric AKI are actually from single center's data. There is also a lack of information concerning AKI patients who did not require CRRT.

Objective: The aim of the study is to: describe pediatric AKI patients, identify risk factor for AKI progression, evaluate the influence of fluid overload and type of fluids administered (colloids, vs crystalloids vs nutrition) on clinical outcomes in AKI (w and w/o RRT) patients, describe current practices of RRT.

Design/Methods: We developed a web-based password protected registry, dedicated to pediatric patients to support an observational and prospective international multicenter study in pediatric intensive care units pICU. Inclusion criteria: all patients admitted to pICU for almost 48 h. We daily collect the amount of fluids (intake and output), diuretics, drugs, vasopressors and inotropes as well as scores and type of ventilation. Sepsis has also a dedicated section. RRT page includes dose calculation, circuit type and life, anticoagulants, type and location of catheter. Treatments done with the new carpediem machine also find their location in this section.

Results: After usability test, the registry has been designed on an open source based framework. Automated data verification system, pRIFLE calculation and alert, fluid management graph result as valid supports for fast data analysis helping in daily clinical activities.

Conclusions: The PAKI registry could represent a step forward in the description of the AKI epidemiology in pediatric patients and contribute to the resolution of the controversies regarding CRRT like initiation, dose, technique, anticoagulation.

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Direct Hemoperfusion with Lixelle S-35: Can Be a New Option of Hyperbilirubinemia Treatment?

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Background: Critically ill patients with acute liver failure (ALF) and acute on chronic liver failure (AoCLF) have limited, complex and expensive options of treatment. For these reasons we

Fig. 1. (for Abstract 23).

Table 1. Bilirubin adsorption kinetics (for Abstract 24)

Type of Bilirubin and Matrix	Ratio Cpout/Cpin t[10 min]	Ratio Cpout/Cpin t[30 min]	Ratio Cpout/Cpin t[60 min]	Ratio Cpout/Cpin t[120 min]
TBIL Plasma	0.91	0.97	0.97	0.98
TBIL Blood	0.92	0.95	0.97	0.99
DBIL Plasma	0.90	0.96	0.97	0.98
DBIL Blood	0.94	0.96	0.97	0.98

TBIL = Total bilirubin; DBIL = direct bilirubin; Cpout = is a concentration of bilirubin outlet the cartridge; Cpin = is a concentration of bilirubin inlet the cartridge.

decided to explore the bilirubin removal capacity of Lixelle S-35 adsorber cartridge through an in vitro test by direct hemoperfusion (DHP).

Methods: We tested two separate hyperbilirubinemic bags contain plasma and blood obtained from a plasmapheresis and exchange transfusion, respectively. The total bilirubin (TBIL) and direct bilirubin (DBIL) were assessed with Jendrassik-Grof method. All tests were performed in triplicate. TBIL and DBIL baseline concentrations were 17.57 ± 0.53 , 12.57 ± 0.23 mg/dL for plasma 23.10 ± 0.47 , 15.37 ± 0.24 mg/dL for blood. Mock DHP was performed for 120 min for each bag at flow rate 100 ml/min. TBIL and DBIL levels were measured at 10, 30, 60 and 120 min for samples drawing from inlet and outlet the cartridge.

Results: On mass balance analysis TBIL and DBIL adsorption onto Lixelle polymer beads were 958.20 ± 5.72 , 680.70 ± 10.68 mg in plasma and 1233.60 ± 10.22 , 818.10 ± 4.68 mg in blood, respectively.

Although, TBIL and DBIL baseline levels decreased rapidly at the beginning of experiments (10 min) they reach plateau subsequent to DHP (120 min) [table 1]. At the end of tests TBIL and DBIL levels were 7.67 ± 0.47 , 5.17 ± 0.17 in plasma and 8.37 ± 0.58 , 5.37 ± 0.39 in blood, respectively.

Conclusion: The in vitro bilirubin adsorption capacity and kinetic of Lixelle S-35 were found to be apparently superior than in vivo available techniques along less complex and expensive benefit (DHP technique). This bench to bedside approach has shown that Lixelle S-35 should be represent an option for the management of hyperbilirubinemia.

Glycopeptides Pharmacokinetic Comparison During Direct Hemoperfusion by Lixelle Adsorption Column

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Background: Different pharmacokinetic properties characterize the two most common Glycopeptides used in clinical setting: Vancomycin (VAN) and Teicoplanin (TEC). Extracorporeal therapy is additional kinetic parameter which can extent this disparity. Thus we set up an in-vitro study in order to investigate VAN and TEC adsorption removal by direct hemoperfusion (DHP) with Lixelle S-35 cartridge.

Methods: We performed a 120 min mock DHP using VAN and TEC solutions (46.08 ± 0.81 and 74.79 ± 1.24 mg/L per N = 6). Antibiotic solutions were circulated in a closed DHP circuit using adsorption column (Lixelle S-35) at flow rate 250 ml/min. Samples were taken at 10, 60 and 120 min from inlet and outlet the cartridge. Drug levels were measured with particle enhanced turbidimetric inhibition immunoassay and fluorescence polarization immunoassay for VAN and TEC, respectively. All tests were performed in triplicate.

Results: VAN baseline levels [fig. 1] decreased rapidly during the first ten minutes of DHP than reaches plateau at sixtieth experiment minute: the total mass adsorbed onto Lixelle polymer was 45.68 ± 2.26 mg. The observed reduction of TEC levels greatly exceeded that of VAN at first interval (10 min) [table 1]. Indeed, the total mass of TEC introduced into the system was completely adsorbed after 1 hour by Lixelle cartridge (126.86 ± 0.91 mg).

Conclusion: Based on findings, different pharmacokinetic properties between VAN and TEC have relapse to kinetic adsorption trend. This should be considered when Glycopeptide are used in patients receiving DHP with Lixelle S-35 to avoid potential underdosing: loading dose may be required for both antibiotics. Furthermore, the high Lixelle S-35 sorbent capacity against TEC may represent an option as rescue therapy in accidental overdose.

Fig. 1. Change in arterial-venous concentrations during mock DHP of saline solution spiked with Vancomycin (baseline antibiotic concentration 46.08 ± 0.81 mg/l) (for Abstract 25).

Table 1. Vancomycin and Teicoplanin Levels during DHP (for Abstract 25)

Time [min]	Arterial Concentration [mg/l]	Venous Concentration [mg/l]
<i>Vancomycin</i>		
Baseline Time [0]	46.08±0.81	–
Time [10]	25.67±0.51	22.17±0.68
Time [60]	21.93±0.72	20.47±0.62
Time [120]	21.90±0.77	21.37±0.83
<i>Teicoplanin</i>		
Baseline Time [0]	74.79±1.24	–
Time [10]	11.98±0.78	LOD
Time [60]	LOD	LOD
Time [120]	LOD	LOD

Baseline concentration samples collected from bag at the beginning of DHP. Vancomycin and Teicoplanin arterial and venous levels at time 10, 60 and 120 minutes. LOD indicates low Limit Of Detection.

In Vitro Cytotoxic Effect of Bisphenol A Released from Hollow-Fiber Hemodialyzers

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Introduction: Bisphenol A (BPA) is an environmental hormones or endocrine disrupting molecular compound. Thanks to its chemical structure that gives good mechanical, thermal and optical properties, BPA is used for the production of some plastics. In particular, in many dialyzers, polycarbonate (PC) of the housing and polysulfone (PSu) of the membranes are plastics based on polymerization of BPA. However, the release of BPA into the extracorporeal circuit may due to cytotoxic events for blood components. Consequently, dialyzers made of different materials may avoid or reduce the BPA elution into the blood of the patients.

Aim of the Study: We compared *in vitro* viability, necrosis and apoptosis on monocytes cell line deriving from BPA elution using two dialyzers made of different materials.

Materials and Methods: We compared dialyzer 'A' (polypropylene housing and polynephronTM membranes) versus dialyzer 'B' (polycarbonate housing and PSu membranes).

We circulated in *in vitro* circuit 600 ml of cells medium for 240 minutes, repeating the same experiments using the 2 different dialyzers. We incubated monocytes cells for 24 hours in medium samples taken before and after the treatments and we evaluated the differences between viability, necrosis and apoptosis of the cells (Navios flow cytometer) in the 2 dialyzers. We also measured the correlation between BPA concentration (true ELISA analysis) and its toxicity on cells.

Results: The results (N = 7) are summarized in the following figures (mean $\pm$ standard deviation):

Dialyzer 'A' seems to release less BPA than dialyzer 'B': the viability of the monocytes is higher, necrosis and apoptosis are lower. The BPA cytotoxicity is evident in the correlation curve with viability, necrosis and apoptosis.

Conclusion: Viability, necrosis and apoptosis of monocytes are influenced by BPA concentration. Use of alternative polymers for dialyzer's components may reduce this cytotoxic effect. However, a direct measurement of BPA concentration in circulating fluid is necessary.

Fig. 1. Results: of the *in vitro* BPA effect on monocytes (N = 7) (for Abstract 26).

Fig. 2. Correlation curve between BPA concentration and cell toxicity (for Abstract 26).

Table 1. Specifications for RD on-the-market devices (for Abstract 27)

	Symplicity™ Renal Denervation System	St. Jude Medical's EnligHTN™ System	Vessix's V2™ Renal Denervation System	Covidien's OneShot™ System	Terumo's Iberis™ System	Recor's Paradise™ System
Power source	RF	RF	RF	RF	RF	US
Catheter size	6F	8F	8F	7–8F	4F	6F
Catheter length	90 cm	115 cm	90 cm	74 cm	155 cm	100 cm
Type of power source	Single tip electrode	4 electrodes at a nitinol basket-like	Array of bipolar electrodes	Balloon with continuous spiral electrode	Single tip electrode	One ultrasound transducer inside an inflatable low-pressure over-the-wire balloon
Max temperature	75°C	75°C	68°C	60°C	70°C	68°C
Max power	5–8 Watt	6 Watt	1 Watt	25 Watt	8 Watt	12 Watt
Time	2 min/ablation	90 sec/ablation	30 sec/ablation	2 min/ablation	2 min/ablation	30 sec/ablation
Number of recommended ablations	4 ablations per artery	8 ablations per artery	1/2 ablation per artery	1 ablation per artery	4–6 ablations per artery	2 ablations per artery
Access	Femoral	Femoral	Femoral	Femoral	Radial	Femoral
CE mark	February, 2008	December, 2011	February, 2012	April, 2012	April, 2013	2012

27**Renal Denervation: Technical Aspects and Future Issues**

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Introduction: Resistant hypertension is defined as the condition where 'therapeutic strategy includes appropriate lifestyle measures plus a diuretic and two other antihypertensive drugs belonging to different classes at adequate doses fails to lower systolic blood pressure (BP) and diastolic BP values to <140 and 90 mm Hg, respectively'. In the case in which the patient presents resistant hypertension, Renal Sympathetic Denervation might represent a novel solution. Catheter-based Renal Denervation (RD) is a minimally invasive procedure involving the delivery of a radiofrequency energy along 1–2 cm in the main renal arteries to ablate the renal nerves located in the adventitia. When the impedance is stable, radiofrequency of controlled energy is applied and an alternating electric field generates a current flows through the electrode; heat is produced because biological tissues acts as a resistor, enhancing the temperature at around 65–70°C and leading to nerves ablation.

RF Device Equipment: A RF device is substantially made of a catheter for the insertion and the application of the electrical signal, one or more electrodes at the tip of the catheter, from which the energy is delivered to the tissue and a RF-waves generator.

Devices on the Market: Several devices have been approved for this procedure and have been used for renal denervation purposes in human beings, but not all are on the market. Radio-frequency (RF) ablation has been the main technology. On the other hand devices exploiting ultrasounds, radiations, nano particles, cryoablation and localized drug delivery are in development. The devices on the market are summarized in the following table.

Conclusion: Even if many aspects have to be investigated, RD seems to be a very promising procedure to reduce resistant hypertension. Industries are highly investing on technological development exploring different and new techniques that in future can allow a complete safety for the patients.

Table 1. Laboratory findings during hospitalization of a 42 year-old male patient with degloving injury (for Abstract 28)

Day	1	2	3	4	5	6	7	8	9	12	15	18	23	26
Urea (mg/dl)	21	14	11	14	15	23	30	44	66	47	22	16	17	12
Creatinine (mg/dl)	1.28	1.15	0.97	1.12	1.0	1.53	1.9	2.79	3.4	2.46	1.83	1.41	1.27	1.12
Potassium (mEq/l)	4.9	4.0	3.3	3.9	3.5	3.9	3.5	5.3	4.8	3.6	3.3	4	4.4	4.1
Sodium (mEq/l)	142	141	145	128	148	147	148	153	153	141	138	139	134	134
Hematocrit (%)	29	29.2	23.6	21.3	22.9	21.7	24	28.8	25.7	23.8	22.5	22.9	20.6	25.2
Hemoglobin (g/dl)	9.8	10.2	8.2	7.7	7.8	7.7	8	7.7	8.5	7.8	7.8	7.6	7	8.7
White blood cells (x 10 ⁹ /l)	9.90	8.19	6.52	4.83	7.38	7.65	8.77	9.67	10.28	8.7	8.9	8.69	5.79	4.6
Platelets (x 10 ⁹ /l)	232	123	83	84	103	115	151	206	256	320	380	446	313	257
Prothrombin time	13.30	17.60	13.00	13.90	12.40	13.10	12.70	12.30	12.30	12.00	10.96	10.90	10.90	12.50
Partial thromboplastin time	33.00	35.20	34.40	38.70	33.60	33.50	31.30	31.00	32.00	33.40	32.90	31.10	31.90	35.20
ALT (IU/l)	24	19	20	24	27	25	21	22	19	27	45	71	56	58
Direct bilirubin (mg/dl)	0.8	2.86	2.88	5.66	4.59	6.06	7.06	8.05	8.24	6.07	2.32	1.38	0.94	0.97
Total bilirubin (mg/dl)	1.52	5.54	4.03	4.05	6.00	8.28	9.48	11.52	11.47	8.81	3.06	1.89	1.29	1.58
Serum myoglobin	700	680	630	420	183	240	305	450	633	2,404	1,182	673	568	300
Urine myoglobin	1,400	1,200	1,260	600	127	96	73	61	80	126	120	99	74	50
LDH (IU/l)	294	258	187	188	186	199	231	272	295	277	243	225	244	249
CK (IU/l)	2,181	2,295	3,165	2,220	1,236	631	320	167	487	129	110	44	50	45

AST = Aspartate amino transaminase; ALT = alanine amino transaminase; LDH = lactate dehydrogenase; CK = creatine kinase.

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Crush Syndrome Consequent to Degloving Injury

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Background: Degloving is a high-energy injury characterized by an exposure to compressive, torsion and tangential forces and a transfer to soft tissues and bones. Therefore, the soft tissue injuries may be very extensive and consist in detachment of skin and subcutaneous tissue from underlying muscles and fascia as well as rupture of perforating vessels. Crush trauma to the extremities, even if not involving vital organs, could be a complication. Crush syndrome, the systemic manifestation of the breakdown of muscle

cells with release of contents into the circulation, leads to metabolic derangement and acute kidney injury.

Case Presentation: We present the case of 42 year-old male suffering from serious circumferential degloving injury, involving two thirds of right lower limb circumference, after being dragged by a forklift during work. The avulsed flap was re-attached in situ and compressive garments were done. It does not bring expected results. He developed a hypovolemic shock, a compartment syndrome of his lower extremity and crush syndrome with high serum creatine kinase (CK) values up to 2181 U/L. After few days, he required lower limb amputation and CVVHDF (high flux membrane) because of kidney injury and metabolic derangement. After 1 week, CVVHDF was discontinued and, after 2 weeks, Creatinine, CK and Myoglobin had almost normalized.

Conclusions: Early, aggressive resuscitation with intravenous fluids in the prehospital setting is recommended to reduce the complications of crush syndrome. Prompt fasciotomies should be performed only when compartment syndrome is present. Treating the patient presenting degloving injuries is difficult and requests a multidisciplinary approach with concurrent monitoring for signs of a developing compartment syndrome.

CVC Microbiological Screening in Vicenza Hemodialytic Population

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Introduction: catheter-related bloodstream infections (CRBI) in hemodialysis (HD) are a relevant clinical issue, and represent the main complication of the vascular access in the HD population. Even though a correct catheter nursing remains fundamental, strategies for microbiological monitoring should be used to reduce the incidence of central venous catheter (CVC) infections in HD patients.

Design: we conduct a retrospective analysis examining microbiological tests in the population treated with HD in our center during 2013 with a tunneled CVC; only patients who did more than 12 HD treatments/year and with age > 18 years were considered. They were monthly monitored for microbiological status with 7 tests: nasal swab (NS), skin swab from exit site (ISSS), intracatheter swab from venous (ES-V) and arterial hubs (ES-A) and 3 paired blood samples from arterial (BS-A) and venous catheter hubs (BS-V) and peripheral vein (BPV).

Results: in 2013 the whole hemodialytic population consisted in 190 patients with 23347 total number of HD treatment, the vascular access used for HD was AV fistula in 155 patients and tunneled CVC in 35 subjects, (total CVC days 7219; mean CVC duration per patient 206). In this last group only 10 subjects (see table 1) presented a positivity in the microbiological screening: BS-A was positive in 4 patients (pt n 7, 8, 9, 10) and one patient (n 9) had 2 distinct episode of positivity from the same hub; only one patient (n 10) resulted contemporarily positive from both branches and peripheral blood. The nasal swab was positive in 5 patients and the exit site swab in 2 subjects; there was no relationship with the positivity of hemocultures or intracatheter swabs.

Conclusions: The regular microbiological monitoring of the CVC in HD population can help to reduce dramatically the episodes of CRBI. In our population the absence of correlation between positive nasal swab or exit site swab has to be related to the prompt detection of the microbiological positivity and to the consequent topic antibiotic therapy; the hemocultures were positive only in critical and immunodepressed patients (pt 7, 8, 9, 10). Our monitoring policy demonstrated high efficacy in CRBI prevention. To further improve this strategy we are studying the association of the monitoring with new antimicrobial lock therapy.

Fig 1. Vascular access in Vicenza HD population and microbiological positivity (for Abstract 29).

Table 1. Episodes of microbiological positivity in HD patients with CVC (for Abstract 29)

	BS-A	BS-V	BPV	ES-A	ES-V	ISSS	NS
Patient 1							1
Patient 2							2
Patient 3							3
Patient 4							3
Patient 5						1	
Patient 6						1	2
Patient 7	1			1			
Patient 8	1			1			
Patient 9	2			2			
Patient 10	1	1	1				

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Modalities of Renal Replacement Therapy, Filters and Anticoagulation in 8 ICUs; An Epidemiology Study

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Introduction: Acute kidney injury (AKI) has always been a challenge in the critically ill, with varying incidence between 3 and 25% depending in the criteria used to define it and the population studied. Some of these patients will worsen their renal function and will require renal replacement therapy. Using continuous methods over intermittent in Intensive Care Units has become an international agreement, especially in hemodynamically unstable

patients. Beside the modality (i.e. intermittent vs continuous), the prescribing physician must decide type of filter, modality and anticoagulation along with other parameters. We describe data from 8 ICU regarding this factors.

Methods: Data from 8 mixed ICU's was retrospectively analyzed in order to describe descriptive statics for modalities, type of filters and anticoagulation. Consecutive patients who were admitted from January 2012 through December 2013 and received RRT were included.

Results: 905 patients were included in the analysis. The used modalities were CVVHDF in 731 patients (80.77%), CVVHD in 35 subjects (3.86%) and CVVH in 139 patients (15.35%). Filters varied among the patients, the most common was High Flux 723 times (79.88% —oXiris® 24 patients—), High Cutoff in 150 treatments (16.57%—150 SepteX®—), HemoPerfusion in 24 patients (2.65%), and low flow filters in 8 patients (0.88%). Most of patients received treatment with heparin in 714 treatments (78.89%), citrate/calcium in 103 patients (11.38%) and no anticoagulation in 88 cases (9.72%).

Conclusion: Modalities of RRT varied among this 8 ICU's. Given that guidelines in these matter are still not available, epidemiologic studies like this might help in development of prospective studies for the creation of useful global databases.

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New Approach to Early Detection of Sepsis: Use of CD64

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Background: Hemodialysis and peritoneal dialysis adult patients are more susceptible than general population to infections and overall to sepsis. This cause of ESRD, comorbidities and the presence of central venous catheter and/or peritoneal catheter. The early diagnosis of sepsis and the consequent timely appropriate treatment is extremely important in order to improve outcome in these patients. The study of suitable biomarkers can have an important impact in the performances of diagnostic tools and could be useful for prognosis and follow up of septic patients during antibiotic treatment. Our goal was to evaluate the clinical usefulness of several biomarkers in terms of fastness and reliability.

Table 1. (for Abstract 30)

Filter	Modality	Heparin	Citrate	No-anticoagulation	Total
High flux	CVVH	129	3	7	139
	CVVHD	5	3	1	9
	CVVHDF	446	84	45	575
Low-flux	CVVHDF	6	1	1	8
High cutoff	CVVHD	25	0	1	26
	CVVHDF	96	0	28	124
Hemo-perfusion	CVVHDF	7	12	5	24
Total		714	103	88	905

Fig. 1. (for Abstract 30).

Table 1. (for Abstract 31)

	Specificity	Sensitivity	Fastness	Cheap
CRP	–	+	++	+
PCT	±	±	++	–
IL-1	–	+	–	--
IL-6	–	+	–	--
TNFα	–	–	–	--
CD64	++	++	--	--

Method: Our research was based on literary search in *PubMed* database using predefined keywords and MESH terms in order to identify clinical and experimental studies evaluating biomarkers and laboratory tests for early detection of sepsis. Only articles on molecules with high sensibility or specificity had been included. Fastness, economic and feasibility characteristics had been also evaluated.

Results and Conclusions: More than 150 biomarkers were compared evaluating their use in sepsis. Most of them had been tested clinically, primarily as a prognostic markers, while few have been used for diagnosis. None has sufficient specificity or sensitivity to be routinely employed in clinical practice. C-reactive protein (CRP) and Procalcitonin (PCT) have been most widely used, but they still have limited ability to distinguish sepsis from other inflammatory conditions or to predict outcome (table 1).

Considering the clinical efficacy of the evaluated biomarkers, CD64 was identified as a potential biomarker able to recognize the infective etiology when a clinical syndrome of systemic inflammation is observed. It showed a correlation with APACHE II and SOFA scores and in particular, the analysis of specificity sensitivity and showed respectively a value of 0.91 (95% confidence interval (CI) 0.85–0.95) and 0.79 (95% CI 0.70–0.86). Currently this biomarker is detected with flow cytometry. This method is reliable but not fast, so further studies on new approaches for rapid CD64 detection are desirable.

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Renal Function Reserve in Healthy Young Subjects Using 1 gm/kg Body Weight Oral Protein Load

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Introduction: RFR(RFR) represents the capacity of the kidney to increase glomerular filtration rate (GFR) in response to certain physiological or pathological stimuli or conditions. Once baseline GFR is determined, RFR can be assessed clinically by oral protein load or intravenous amino acid infusion. The baseline GFR measured routinely gives a functioning status of an individual kidney at a particular time and metabolic state which doesn't gives the actual value of maximum GFR which can be attained by that individual under 'stress'. Studies has been done in past to determine the renal function reserve of subjects using either fixed protein load or using amino acid infusion.

We did an observational study among 18 young healthy individuals for the evaluation of the renal function reserve with a protein load of one gram per kilogram body weight, there were 10 males and 8 females.

Results: In order to evaluate the differences of GFR observed before and after protein load (PL) a Mann Whitney test was performed in all considered subject and then in male and female subject Data are expressed as median [I-III interquartile] and p value. A p value <0.05 was considered statistically significant (table 1 and figure 1).

Fig 1. Shows the median value [I-III interquartile] of GFR before and after protein load(PL) (for Abstract 32).

Table 1. Differences of GFR (expressed in ml/min/1.73 m²) in groups before and after protein load (for Abstract 32)

Average	Before Protein load	After Protein load	p
All subjects	101,36 [97,22; 108,55]	139,64 [123,23; 165,69]	<0.0001
Males	98,06 [96,36; 104,11]	134,81 [119,12; 161,53]	0.0003
Females	109,98 [99,61; 117,98]	147,46 [132,93; 165,27]	0.0034

Conclusion: With this study we found there can be large variation in the stress GFR and the renal function reserve among individuals, males and females. These variations in the stress GFR and RFR can be used to make an ideal standard stress test for kidney to predict risk of acute kidney injury and future risk for chronic kidney disease, and to uncover possible loss of renal functional mass.

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Impact of Lifestyle and Family History on RFR in a Young and Healthy Sample

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Background: For diagnosis and follow-up of kidney diseases, the most common way is measuring or estimating GFR, but its results may not show the real condition or total capacity of the kid-

ney. In this way, the concept of Renal Function Reserve (RFR) can be useful. It shows not a steady state of the kidney, but a dynamic renal function and can be reached after a stress test, when the kidney utilizes its ability to maintain his function even in adverse moments. It may be used in CKD context for early diagnosis, for follow up or to show who are those in increased risk. But the determinants and variables of RFR through different demographic characteristics and clinical conditions, as well as lifestyle, are not well known.

Methods: So we observed the baseline GFR, the maximum GFR and the RFR of 18 healthy young volunteers (10 men and 8 women) between 23 and 40 years old, dividing them by family history of diabetes and hypertension, smoking, and amount of physical activity (PA). For the RFR we did a protein load of 1 gram/kilogram of weight, measured renal function before and after and took the difference as the renal reserve. For PA we utilized the IPAQ (self-administrated) score, where all results were moderate (9 subjects) or high (9 subjects) amount of PA.

Results: Between the different groups, respectively the median of: baseline GFR, maximum GFR (after protein load) and RFR, in ml/min/1.73 m², were: moderate amount of PA: 103.80, 136.44, 28.82; high amount of PA: 98.17, 164.95, 50.08; no smoking: 101.35, 133.52, 27.69; smoking: 101.33, 159.80, 50.51. The median RFR when personal family history is analyzed: No DM and DM history: respectively 36.70 and 28.82 ml/min/1.73 m², and no hypertension and hypertension family history: 27.22 and 39.22 ml/min/1.73 m², respectively. The median RFR among men was 37.76 and among women was 29.72 ml/min/1.73 m².

Conclusion: This results trends to show a bigger rise on GFR and also a larger RFR among those with more intense weekly PA. Also, smokers trend to have a superior improvement on GFR and a bigger RFR. In both of this the basal GFR were the same. Family histories of hypertension or DM does not seem to relate to changes in RFR among young healthy individuals.

Despite the small number of subjects, we conclude that there may be a positive relationship between the amount of physical activity and increase in GFR or RFR and between smoking and improvement of GFR or RFR. We can't say the same of family history of hypertension and diabetes. Studies with a larger number of subjects are necessary to confirm these premises.

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The Role of BIVA in the Management of Fluid Status in HD Patients

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Background: In hemodialysis patients the optimal fluid management is achieved by adjusting post-dialysis target dry weight and by excess fluid removal using ultrafiltration. Ideally, HD patients should remain in normal hydration status throughout the

Fig. 1. GFR and RFR x Physical Activities (for Abstract 33).

Fig. 2. GFR and RFR x Smoking (for Abstract 33).

Fig. 1. Hydration status of study population (for Abstract 34).

interdialytic period, without excessive fluctuations between dehydration and fluid overload. There are some clinical parameters that guide in the prescription of target weight (edema, muscles cramps, blood pressure (BP) etc.), but sometimes the signs of fluid status are ambiguous. Therefore, a dry weight clinically established, without objective data, could lead to cramps, asthenia and other complications and compromise the Residual Renal Function (RRF), that is a powerful predictor of survival both in PD and HD population. In NECOSAD Study, there was demonstrated that episodes

Table 1. Hydration status of study population (for Abstract 34)

	Diuresis (18 pt)			No Diuresis (44 pt)			Total (%)
	Pt (%)	Hypotensive episodes (mean)	BNP (mean)	Pt (%)	Hypotensive episodes (mean)	BNP (mean)	
NH	77.8	0.64	8,000	50	1	10,000	58.1
DH1	5.6	0	3,600	2.3	1	15,000	3.2
DH2	0	0	0	0	0	0	0
DH3	0	0	0	6.8	1	10,500	4.8
HH1	11.1	0	8,000	22.7	1.2	13,000	19.4
HH2	5.6	6	19,714	18.2	3.75	22,800	14.5
HH3	0	0	0	0	0	0	0

of volume depletion and intradialytic hypotension were an independent risk factor for the loss of RRF in HD.

Technology provides useful objective information about fluid status through Bioelectrical Impedance Vector Analysis (BIVA). In our clinical practice we use BIVA for determination of the ideal dry weight, that is usually adjusted according both to clinical signs and to BIVA results.

The aim of this observational study is to characterize the benefit of BIVA-guided fluid management in HD patients, for maintaining normal hydration and hemodynamic stability.

Methods and Results: We studied 62 patients, in maintenance hemodialysis in San Bortolo Hospital in Vicenza. We divided the population in two groups: with residual diuresis (>200 ml/24 h, measured in the day before dialysis session) and without residual diuresis. For each patient, BIVA measurement was performed at the end of dialysis session, when they reach established dry weight.

Patient's body fluid status was classified into three main categories: normal hydrated (NH), between 72.7% and 74.3%, dehydrated (DH), <72.7%, and hyper hydrated (HH) >74.3%; the last two categories are further subdivided into mild (DH1, HH1), moderate (DH2, HH2) or severe DH3, HH3. In each patient we also measured the blood pro NT-BNP, and evaluated the number of intra dialytic hypotension episodes (decrease in systolic BP by ≥ 20 mm Hg or a decrease in MAP by 10 mm Hg associated with symptoms) in the current month. Results are showed in table 1, figure 1.

Conclusions: Using BIVA-based dry weight prescription, 58.1% of our HD population is normal hydrated. The patients with residual diuresis are more euvoletic than anuric patients, in which there are more hyper-hydrated subjects. HH status, in patient both with diuresis and anuria, is associated with hemodynamic instability and cardiac stress. It is important to maintain a normal hydration status and to avoid both hypervolemia and hypovolemia, which are correlated with hemodynamic instability. It should be convenient the implementation of bioimpedance measurement as dry weight estimating method in order to assess individual euvoletic. Future prospective study results are needed to confirm the role of normal hydration status in urine output preservation in HD patients.

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Peritoneal Ultrafiltration and Refractory Congestive Heart Failure. Is It Still Relevant as Idea?

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Introduction: Heart failure (HF) is a serious disease that affects 1–2% of the adult population in developed countries with a prevalence rising to more than 10% among people aged over 70 years.

End-stage congestive HF can become refractory to medical treatment even in patients with normal renal function. These patients require frequent hospitalizations for dyspnea, orthopnea, paroxysmal nocturnal dyspnea, electrolyte imbalance and oliguria. In patients with HF, neurohormonal activation leads to fluid overload that may be treated by means of high doses of furosemide until hyponatremia and diuretic resistance occur and anti-aldosterone drugs that can produce hyperkalemia. In some cases of refractory HF, ultrafiltration (UF) is needed. Extracorporeal UF may be indicated as emergency treatment of severe refractory congestive HF. Its limits are the possibility of developing hemodynamic instability and severe hypotension. For a selected HF population, it is also available a different management using peritoneal UF. To perform this technique, it's mandatory a cooperation between cardiologists and nephrologists to plan:

- Surgical placement of a peritoneal catheter;
- Training of the patient or a caregiver to the peritoneal dialytic exchanges;

The use of intraperitoneal solution like icodextrin promotes a good peritoneal UF during a nighttime dwell of 10–12 hours. This slow UF is more tolerated by the cardiological patient with an improvement of the life quality.

Literature Review: Reports on peritoneal UF in HF without end-stage renal disease (table 1).

Conclusion: End-stage congestive HF frequently becomes refractory to medical treatment and undergoes recurrent clinical worsening that requires prolonged hospitalizations with high mortality rate and costs. On the basis of the literature data, peritoneal

UF preserves better residual renal function, is less invasive, improves clinical symptoms and life quality with less adverse events than extracorporeal UF. Thus, it seems reasonable to propose this technique as a palliative therapy for the long-term ambulatory management of refractory congestive HF patients. However, since these results derive from small case series, randomized controlled trials, with either cardiological and nephrological supervision, are needed to assess peritoneal and/or extracorporeal UF for the treatment of HF in comparison with pharmacological treatment.

Table 1. Reports on peritoneal UF in HF without end-stage renal disease (for Abstract 35)

Schneerson SJ.	1949	Case report	1
Mailloux LU.	1967	Case series	15
Konig P.	1991	Prospective, non-randomized	13
Ryckelynck JP.	1997	Prospective, non-randomized	16
Bilora F.	2002	Prospective, non-randomized	16
Aggarwal HK.	2002	Retrospective	20
Ortiz AM.	2003	Case series	3
Gotloib L.	2005	Prospective, non-randomized	20
Salvatori G.	2006	Case report	1
Phadke G.	2008	Case report	1
Próchnicka A.	2009	Case report	1
Sánchez JE.	2010	Prospective, non-randomized	17
Sotirakopoulos NG.	2011	Prospective, non-randomized	19
Bielińska Ogrodnik D.	2013	Case report	1
Próchnicka A.	2013	Case report	1
Bertoli SV.	2014	Retrospective	48

Table 1. Differences of data treatment among groups (for Abstract 36)

	Citrate (72 pts)	Heparin (537 pts)	No-anticoagulation (62 pts)	<i>p</i>
Entire time of treatment (hrs)	33.20±22.6	29.04±25.36	27.29±23.67	0.30
Effective time of treatment (hrs)	31.06±19.73	26.24±17.89	24.68±19.38	0.04
Downtime (%)	4.90±3.06	6.92±4.05	7.51±4.74	<0.001
Delivered dose (ml/kg/hr)	40.10±3.2	34.9±6.7	27.7±9.2	<0.001
Delivered/Prescribed dose (%)	89.1	77.5	61.5	<0.001
Number of TMP/DP warning (mean ± SD)	0.14±0.87	0.69±2.39	1.38±3.50	0.01

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Downtime, Doses and Clotting Complication Among Continuous Renal Replacement Therapy Performed with Different Anticoagulation Techniques:

A Preliminary Retrospective Study

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Introduction: The need for continuous anticoagulation represents a potential drawback of Continuous renal replacement therapy (CRRT). Despite the most recent KDIGO guide lines suggests to use regional citrate anticoagulation in patients without contraindications, systemic unfractionated heparin remains the most used anticoagulation during CRRT. Aim of this study is to retrospectively evaluate differences in downtime, delivered dose and number of warning related to circuit clotting among treatments performed with citrate, heparin and without anticoagulation.

Method: Data of treatment contained in the memory cards of all CRRT machines of a tertiary hospital were analyzed. According to anticoagulation therapy performed, treatments were divided in a Citrate, Heparin and No-anticoagulation groups. For all procedures the entire and effective time of treatment, downtime, prescribed and delivered doses, numbers of TMP/DP alarms and number of clotted sets were considered. Results are expressed as mean ± SD and differences among groups analyzed through ANOVA. *p* < 0.05 was considered for statistical significance.

Results: Memory cards of 8 CRRT machines (PrismafleX, Gambro Lundia AB) were analyzed and data from 671 treatments, performed from Jan 2012 to Dic 2013, were extracted. Differences in entire and effective time of treatments, downtime and delivered dose are presented in table 1. If compared to prescribed dose, delivered dose was reached in 89.1% of citrate, 77.5% of heparin and 61.5% of no-anticoagulation groups. TMP/DP warning was obtained in 5.55% of citrate, 15.64% of heparin and 25.80% of no-anticoagulation groups. Mean number of TMP/DP warning is presented in table 1. Numbers of sets changed for clotting were 9.72%, 40% and 52% respectively for citrate, heparin and no-anticoagulation groups.

Conclusion: In our preliminary retrospective evaluation, a significant increase in effective time of treatment results for Citrate when compared to Heparin and No-anticoagulation groups. The

Fig. 1. (for Abstract 37).

reduction in downtime allows to reach higher delivered/prescribed dose ratio in Citrate group (89.1%). Considering the reduction of membrane clotting and warning related to extracorporeal circuit clotting, an increase in clearance could also be supposed.

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Methodology for Economic Evaluation of On-Line Hemodiafiltration Versus High Flux Hemodialysis

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Introduction: Empirical evidence suggests that On-Line Hemodiafiltration may lead to better clinical results with respect to High-Flux Hemodialysis. However, randomized studies were not able to support in a conclusive manner the superiority of clinical outcomes related to this more advanced therapy. Several cost analyses were performed in order to assess the differential expenditures between the two therapies.

Aim of the Study: We investigate whether clinical benefits, in terms of longer survival and better life quality, are able to offset the

possibly higher costs related to On-Line HDF with respect to traditional High-Flux HD, and thus whether it is worth investing in this more innovative therapy.

Methods: We build a simulation exploiting existing data from previous randomized studies on On-Line HDF. The first step is to construct a baseline sample of High-Flux HD patients; we use the dataset from the Membrane Permeability Outcome (MPO) Study. We perform a statistical analysis on the survival time data of these High Flux HD patients and we apply a relative risk between On-Line HDF versus High Flux HD, extrapolated from the most relevant randomized studies about this comparison, in order to estimate the corresponding On-Line HDF survival function. Exploiting these results, we build two parallel Markovian models (the structure is shown in the figure below) to generate a simulation comparing the survival of the same sample of patients treated with High Flux HD and On-Line HDF. We then adjust the survival output through the application of Quality of Life coefficients, and we associate to each state of the model the corresponding estimated costs, taken from the literature. Thereafter, we generalize the model with the addition of variability and uncertainty on parameters through (i) a one-way probabilistic sensitivity analysis, varying all the input parameters, such as costs, utilities, event probabilities and treatment effects, over defined ranges, and (ii) a probabilistic sensitivity analysis, performing simulations with parameters defined as distributions and not as fixed values. Afterwards, we run several Monte Carlo simulations for different patients. Lastly, we perform an output analysis through scatter plots of simulations and the estimation of Incremental Cost-Effectiveness Ratios (ICERs) and Cost Effectiveness Acceptability Curves (CEACs).