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Abstracts

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SIRS, Sepsis and MODS

P01

Metabolomic Characterisation of the Effects of CytoSorb in a Cohort of Patients suffering from Multiple Organ Dysfunction Syndrome (MODS)

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Introduction: Cytosorb® technology is an extracorporeal blood purification therapy which rapidly reduces the blood levels of inflammatory mediators and medium molecules.

By interrupting the inflammatory storm, Cytosorb therapy is associated with hemodynamic and organ damage improvement.

Background/Aims: Many studies showed the efficiency of Cytosorb® in the adsorption of pro-inflammatory cytokines, but little is known about the whole metabolic modifications induced by the treatment. Aims of our study protocol are: to describe whole metabolic effects of Cytosorb® through metabolomic analyses; to elaborate a mathematic model correlating significant modification to traditional outcomes, such as ICU-mortality, 30-days mortality, improvement of hemodynamics and of kidney and liver damage.

Materials and Methods: the design of the study is prospective, observational.

Predicted sample size is 40 patients, receiving at least 1 cycle of Cytosorb®, suffering from MODS, defined as the development of progressive and potentially reversible physiologic dysfunction in 2 or more organs or organ systems: pulmonary, renal, hepatic, central neurologic, cardiovascular, and hematologic systems.

Blood samples will be collected at T0, before starting treatment, and T1 = 3 h, T2 = 12 h and T3 = 24 hours after Cytosorb® implementation. Patients' clinical, laboratory and hemodynamic data will be collected at the same time intervals.

Blood must be collected in heparin tubes, centrifuged for 10 min to obtain plasma aliquoted in 1.5 mL Eppendorf Safe-lock tubes. We will mark with permanent marker the sample code on each tube and record in on an Excel file. Then, we will store the samples at –80 °C as soon as possible until analysis. For the analysis of metabolomics data, the Excel data matrix containing patients data versus metabolites will be processed using homemade routines Matlab and R based, the integrated web-based platform MetaboAnalyst 4.0 and the SIMCAP+13, the Umetrics Software.

Results: All the groups of samples from patients affected by different response to the MODS perturbation and Cytosorb therapy will be tested as phenotypes of interest and then used to classify unknown sample before the start of treatment. Metabolites responsible will be revealed, and they will be classified as "finger print" of these phenotypes. Biochemical links between the metabolites will be highlighted and "similarity" of each sample to the phenotypes will be measured in the metabolomics space.

Canonical pathways and perturbation related networks will be analysed. All the biochemical links involving cytokines and other molecules will be analysed. Specific metabolomic profiles related to an optimal outcome of patient will be described and proper pretreatment therapy would be suggested to "prepare" the patients to improve the perturbation response.

Conclusions: Cytosorb indications are expanding. A complete characterization of its performance in modifying the metaboloma could be useful in identifying other than cytokine absorption-related mechanisms, and possibly in predicting the subset of patients one can expect the maximum benefit.

P02

Hemoadsorption with CytoSorb, Single-Center Preliminary Experience

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Background: Sepsis is the most common cause of death in medical intensive care units (ICU). If sepsis progresses to refractory septic shock, mortality may reach 90–100% despite optimum current therapy. One of the hallmarks of sepsis is the excessive release of cytokines and other inflammatory mediators causing refractory hypotension, tissue damage, metabolic acidosis and ultimately multiple organ failure. Cytokine reduction by hemoadsorption represents a new concept for blood purification, developed to attenuate the systemic levels of pro-inflammatory and anti-inflammatory mediators released in the early phase of sepsis.

Methods: We evaluated the impact of a new hemoadsorption device (CytoSorb), used as adjunctive therapy, on hemodynamics and clinically relevant outcome parameters in 20 critically ill pa-

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Table 1. Levels of Procalcitonin, C-reactive Protein and white Cells count all before and after the Treatment (for Abstract no P02)

	Baseline	After hemoadsorbtion
Procalcitonin	31	7
C-reactive protein	67	13
Leukocytes	18.250	12.300
Vasopressor dose mcg/kg/m	4.2	2.3

tients with septic shock and in need of renal replacement therapy (RRT) in Intensive Care Unit. Mean levels of MAP, procalcitonin, noradrenalin need and SOFA score were evaluated. RRT of acute renal failure was performed either as continuous venovenous hemofiltration (CVVH) or continuous venovenous haemodialysis (CVVHD) at the discretion of the attending physician. Flow rates were set to achieve a dialysis dose of 25 ml/kg/h, blood flow rate was set accordingly. Hemoperfusion was started after refractory shock was diagnosed. The adsorber [total volume 300 ml, priming volume 120 ml, filled with sterile normal saline (NaCl 0.9%)] was connected in a PRAE-filter position into the RRT circuit. The first exchange was performed within 24 h without interruption. Further adsorber exchanges were at the discretion of the physicians.

Results: After Cytosorb treatment procalcitonin, C-reactive protein and white cells count all decreased vs basal levels (Fig. 1). This feature was associated with hemodynamic stabilization and a reduction of noradrenaline infusion. SOFA score improved in 7/20 patients, however overall mortality was 75%. Treatment using the CytoSorb device was safe and well-tolerated with no device-related adverse events during or after the treatment sessions.

Conclusion: In severe septic shock unresponsive to standard treatment, haemodynamic stabilization and inflammatory parameters improved using cytokine adsorption therapy. These effects seem to be more pronounced in patients in whom therapy started within 24 h of sepsis diagnosis, whereas a delay in the start of therapy was associated with a poor response to therapy in terms of reduction of catecholamine demand and survival. Detailed studies and registry reports may better define the potential benefits of this new treatment option.

P03

Blood Purification with Cytosorb® in Abdominal Septic Shock: A Case Report

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Background: Cytokines reduction by hemoadsorption represents a new concept for blood purification in septic shock.In the present case report, we evaluated the impact of Cytosorb® hemoadsorption device, used as a weapon in patient-tailored therapy, on macro and micro haemodynamics.

Methods: A 70-years-old man was admitted to emergency department with peritonitis, severe lactic acidosis (serum lactate: 6.8 mmol/L), and imaging was consistent with ureteral rupture after operative ureteroscopy with peritoneal purulence. He underwent a surgical ureteral repair and debridement of the peritoneal cavity.

This patient was admitted to ICU with the diagnose of septic shock, SOFA score was 14, and underwent an adequate fluid resuscitation. Vasopressors were needed to treat hemodynamic instability. Microbiological samples were promptly taken and a broad spectrum antibiotic therapy was started. Procalcitonin levels were elevated: 330 μg/L. We implemented invasive hemodynamic monitoring using Picco2® that showed an adequate cardiac output (Ci 4.69 L/min/m^2), but a reduced systemic resistance (SVRI 903 dynes-sec/cm^{-5}/m^2).We started microcirculation analysis in sublingual mucosa with a non invasive videomicroscopy technique using Cytocam®. A perfused vessel density (PVD) of 15.17 was detected and mean flow index (MFI) was 2.58.

Terlipressin was needed to treat vasoplegic shock that was unresponsive to high dosage of norephinephrine: 2 μg/kg/min. The patient developed an acute kidney failure with anuria that was unresponsive to massive diuretic therapy and continuous veno-venous heamodialysis (CVVHD) was started.

Admission blood essays shown severe lactic acidosis accompanied by high levels of cytochines: IL1 5 pg/ml, IL6 361 pg/ml, IL8 214 pg/ml, IL10 28 pg/ml, TNF-a 126 pg/ml.

We started a combined treatment of hemoadsorption using a Cytosorb® hemoadsorber and CVVHD.

Results: After 6 hours of treatment we noticed a reduction in plasmatic cytochines levels: IL1 5 pg/ml, IL6 118 pg/ml, IL8 145 pg/ml, IL10 27.8 pg/ml, TNF-a 61.1 pg/ml.

After 24 hours of treatment we described an improved quality of blood flow: MFI 2.75 and increased PVD 16.08. Cytochines levels were reduced IL1 5 pg/ml, IL6 178 pg/ml, IL 8 67 pg/ml, IL10 34.8 pg/ml, TNF-a 38.1 pg/ml. SOFA score was 11. We extended Cytosorb® treatment for 72 hours using 3 cartridges with a restoration of macrohaemodynamic parameters.

Conclusion: We present a case of septic shock with peritonitis leading to multi organ failure.

The early treatment with a combination of CVVHD and Cytosorb® led to a rapid hemodynamic and metabolic stabilization, suggesting that hemoadsorption might be an option in patient-tailored therapy of septic shock.

P04

Clinical Effects of Hemoadsorption with Cytosorb for Septic Shock in a Polytrauma Patient

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Background: Polytrauma represents one of the most frequent cause of death in the young population. Early death may occur immediately due to lethal injuries (i.e. primary brain injuries, aortic rupture, haemorrhagic shock or decapitating injuries) or in the few hours due to consequences of abdominal and intrathoracic bleeding or severe traumatic brain injury; late mortality is often caused by septic complications and multi-organ failure. Indeed, the initial injury promotes a systemic inflammatory response to stimulate reparative mechanism and the subsequent ischemia/reperfusion injury, operative treatments and infections may exaggerate this response, leading to multiple organ failure.

In this field, extracorporeal blood purification through sorbent cartridges, as Cytosorb (Cytosorbents Inc.), represent an adjuvant therapy modulating the excessive inflammatory response.

Case Presentation: We present the case of a male patient. 24 yo. admitted to our hospital with a severe polytrauma resulting in head injuries, thoracic trauma with hemopneumothorax – immediately drained – and abdominal trauma with multiple hepatic lesions. A surgical hepatic packing was used for a rapid hemorrhage control and then the patient was transferred in the Intensive Care Unit.

In the second day, a reoperation was performed to remove the hepatic packing and, hereafter, abdominal CT showed a necrotic area and a biloma formation, a frequent complication in hepatic injuries, treated by performing an endoscopic retrograde cholangiopancreatography (ERCP) and a percutaneous catheter drainage of bile acids.

Then the patient suddenly got worse, presenting a SOFA score of 17, corresponding to a mortality rate nearly of 90%. He developed oliguria (creatinine: 3.47 mg/dl, diuresis: 40 ml/h), hemodynamic instability (mean arterial pressure: 60 mm Hg) sustained by norepinephrine infusion (0.4 μg/kg/min), metabolic alterations (lactate: 4 mmol/L) and respiratory failure. Septic shock caused by *Acinetobacter baumanii* bacteria was diagnosed from pulmonary culture and antibiotic therapy was started administering Colistin (4.5 M 2/day ev), Meropenem (2 g every 8 h ev) and Tigecycline (firstly 100 mg, then 50 mg every 12 h ev).

In front of this clinical condition, a treatment with Cytosorb in combination with continuous renal replacement therapy (Prismaflex, CVVHDF) was started for 4 consecutive cycles, 24 h each.

Results: The treatment resulted in a general improvement of clinical condition (Table 1). The patient showed hemodynamic improvement immediately after the first cycle until its complete stabilization associated with the abolition of norepinephrine after 72 h. Lactate and hepatic enzymes levels stabilized within normal values as creatinine and diuresis, which gradually recovered. Extravascular lung water index levels (EVLW) decreased during the treatment and was related to a SOFA score improvement. The patient could be weaned from ventilator on day 7 and discharged from ICU.

Conclusion: Cytosorb resulted in a rapid hemodynamic stabilization associated with a general patient improvement by controlling the cytokine storm and at the same time supporting the hepatic detoxification.

Table 1. SOFA score and Laboratory characteristics at baseline and during the treatment (for Abstract no P04)

	ICU admission	2nd Day – Start Cytosorb	3rd Day: 24 h	4th Day: 48 h	5th Day: 72 h	6th Day: 96 h	7th Day
SOFA	9	17	15	13	9	10	9
EVLW (ml/kg)	14	13	12	12	10	8	8
CPR (mg/l)	1.8	107.4	146.7	124	96.2	88.7	115.8
PCT (ng/ml)	2.31		9.26	8.32			
Lactate (mmol/l)	3.7	4	1.6	1.4	1.5	1.3	0.9
Norepinephrine (μg/kg/min)	0.4	0.2	0.18	0.06	Stop	Stop	Stop
MAP (mm Hg)	60	60	80	90	90	90	90
Diuresis (ml/h)	40	40	80	80	100	100	150–200
Creatinine (mg/dl)	1.16	3.57	1.79	1.17	1.2	0.81	0.65
Bilirubin (mg/dl)	3.48	5	4.91	–	–	–	–
AST (U/L)	2,475	2,139	920	378	–	179	–
ALT (U/L)	2,349	3,060	1,745	1,145	–	49	–

P05

Early Continuous Haemodiafiltration with Cytokine Adsorption Filter (Cytosorb©) After Kidney Transplant: A Case Report

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Background: Renal replacement therapy (RRT) start timing has been a controversial and debated topic in critical care literature and the optimal time to begin RRT in the setting of sepsis-induced acute kidney injury is still undefined. Nevertheless, especially when the aim is to actively remove cytokine and inflammatory mediators in septic shock (i.e. using Cytosorb© hemoadsorption) an early treatment is of paramount importance. However, a kidney transplant graft is extremely susceptible to any hemodynamic alteration and early RRT could result in delayed graft function, especially in the immediate postoperative period. Therefore, the decision to start RRT with adsorption filter in a septic kidney transplant recipient is extremely challenging. We present a case in which RRT with Cytosorb© was started five days after a kidney transplant for septic shock and the kidney graft function was successfully achieved after treatment's end.

Case Report: A 69-year-old male patient with a history of arterial hypertension, dyslipidemia, glucose intolerance and ischemic heart disease underwent kidney transplantation for chronic kidney disease (CKD) due to nephroangiosclerosis. He was subsequently hospitalized in sub-intensive care unit (SICU) for the postoperative course. During the first and second postoperative days (POD), the patient appeared in good general condition, apyretic, hemodynamically stable, oliguric (0.25 ml/kg/h). In third POD he began intravenous therapy with furosemide 250 mg/day, with a significant increase in diuresis (0.45 ml/kg/h). On the fourth POD he developed fever (38.3° C), hypotension and respiratory failure; the blood chemistry tests showed important leukopenia. The patient was then intubated and transferred to ICU. Therapy with norepinephrine became necessary and empiric antibiotic therapy was started. The diuresis, initially valid (1 ml/kg/h) with furosemide, was subject to progressive reduction. Due to worsening conditions, on the fifth POD furosemide infusion was suspended and RRT (CVVHDF) was started with the first adsorption filter (Cytosorb©). In the same day it was possible to interrupt norepinephrine support. Two treatments in total with Cytosorb© filters were performed and after treatment he appeared apyretic, hemodynamically stable and showed a valid spontaneous diuresis (0.73 ml/kg/h) even on CRRT (Fig. 1). After CRRT was suspended oliguria reoccurred and the patient developed fluid overload, thus CVVHDF was re-initiated. In the following days there was a progressive improvement of respiratory parameters, the blood culture showed an E. Coli infection. At the end of the second CRRT cycle, spontaneous diuresis was resumed after stimulation with furosemide. The patients was extubated on the seventeenth POD and transferred to SICU; at the time of discharge kidney graft function was normalized.

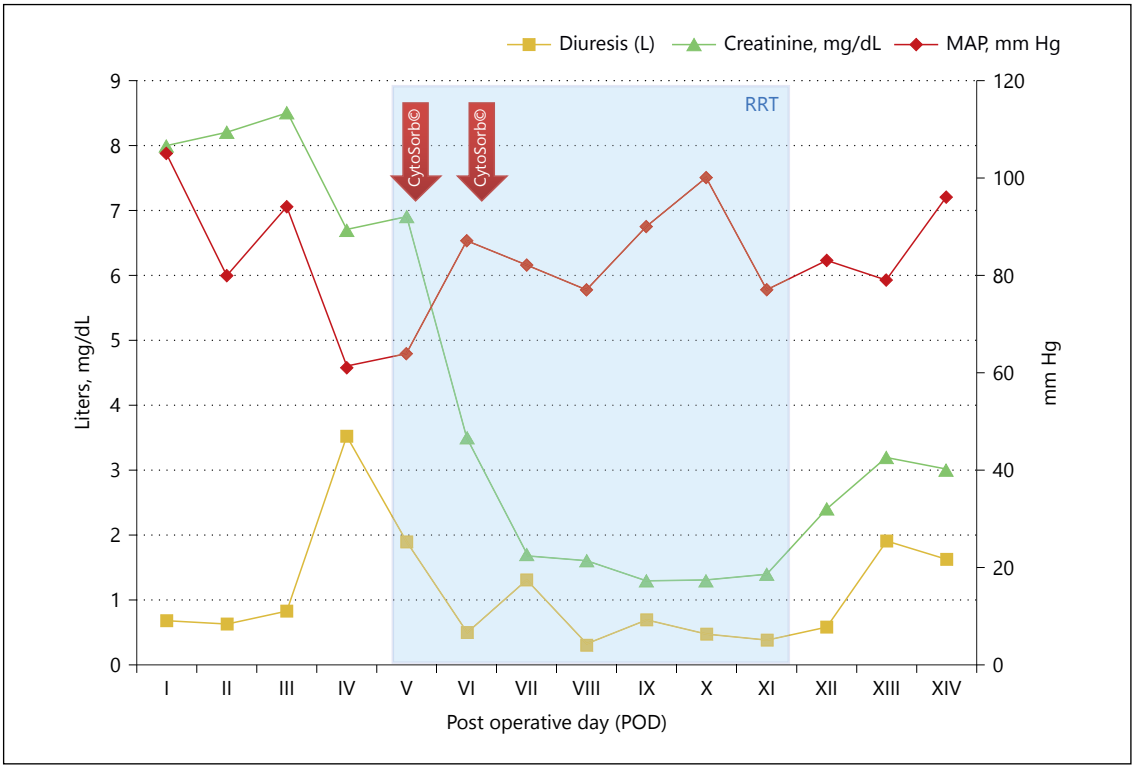

Fig. 1. Course of renal function and hemodynamic during the treatment (for Abstract no P05).

P06

Delayed Graft Function and Immunosuppression Drugs in Kidney Transplant: Cytokine Release Syndrome Succssfully Treated with Adjuvant Hemoadsorption Therapy

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Background: Pre-emptive transplantation is associated with a longer survival and improved quality of life since it can avoid the need of dialysis and its complications. Notwithstanding the advantages, the related risk of delayed graft function (DGF) and acute rejection is not completely absent, especially considering high risk profiles donors and recipients. Furthermore, some pharmacological immune suppression drugs, i.e. Anti-thymocyte globulin (ATG), might present critical adverse effects, above all the Cytokine Release Syndrome (CRS), impacting most organ systems. Therefore, cytokine levels modulation through blood purification could be a possible adjuvant strategy to limit CRS induced injuries and multi-organ dysfunction.

Case Presentation: We present our experience of a young male patient, 23 yo, weight 60 kg, suffering from IgA nephropathy, known as Berger's disease, who underwent to a pre-emptive kidney transplant. In the immediate post-operative days, the occurrence of DGF was observed, firstly treated with Tacrolimus, Mycophenolic acid and subsequently with several administrations of ATG. After 20 days post-transplant, the patient developed a CRS because of a recurrent ATG cycle, resulting in a worsening severe multi-organ dysfunction. The patient was immediately transferred to our ICU with a severe decline in kidney function (creatinine serum: 3.49 mg/dl), metabolic disorders with lactic acidosis (lactate: 4.8 mmol/l), progress to acute respiratory distress syndrome (ARDS) and cardiac dysfunction. An impairment of the hemody-

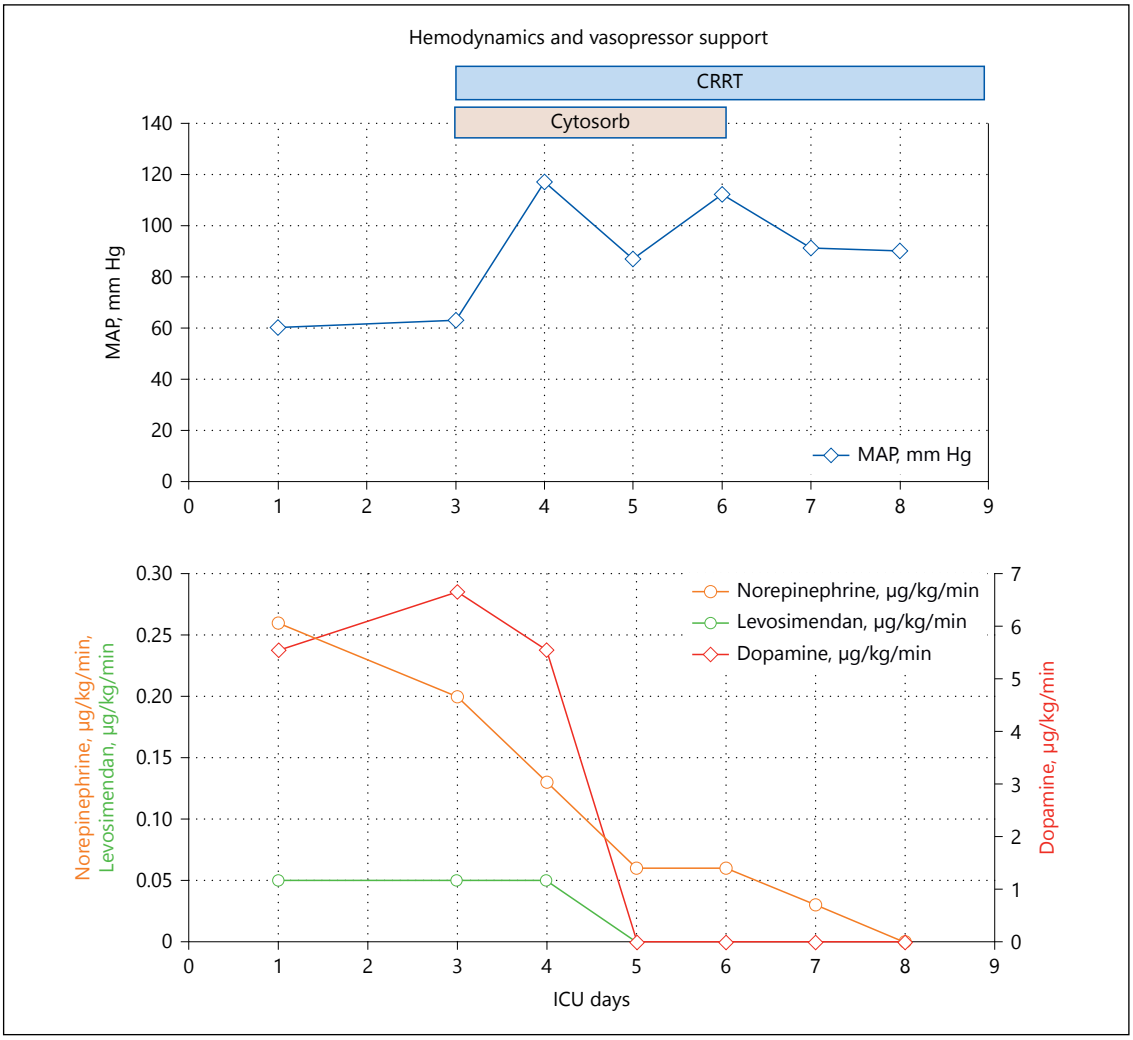

Fig. 1. Hemodynamic improvement and vasopressors support course during the treatment (Day 1: ICU admission) (for Abstract no P06).

namic status was observed (mean arterial pression, MAP: 60 mm Hg), requiring the administering of Norepinephrine (0.26 μg/kg/min), Dopamine (5.55 μg/kg/min) and then also Levosimendan (0.05 μg/kg/min) to maintain an adequate perfusion and contractility. In the third day in ICU, the limited respiratory function deteriorated (P/F: 42) requiring mechanical respiratory support with pressure-controlled ventilation (PCV), whereas in front of the severe impairment of renal function (creatinine: 5.28 mg/dl), CVVH treatment (Amplya, Bellco) was started.

Cytosorb cartridge was additionally installed into the CRRT circuit with the aim of modulating the cytokine cascade involved in CRS and organ dysfunction, trying to control the organ damages and graft rejection. We performed 3 consecutive Cytosorb cycles, 24-h each until a hemodynamic and general clinical improvement was obtained.

Results: The combined treatment resulted in an important hemodynamic improvement (Figure 1), obtaining a quick MAP stabilization, accompanied by a reduction of inotropic support during the course of the treatment until its complete abolition. Renal function was restored and diuresis returned normal and, on day 9, the patient could be extubated.

The SOFA score improved from 17 to 12 at the end of the treatment and the patient was discharged from our ICU on day 13 in a general good clinical condition (SOFA 4).

Conclusion: Our preliminary experience underlines that the use of Cytosorb hemoadsorption cartridge may be helpful to control cytokines involved in CRS caused by DGF and immunosuppressant drugs in order to limit organ-related damages and eventually prevent graft rejection.

P07

CytoSorb for Treatment of Sepsis in Kidney Transplant Recipient: Efficacy and Safety

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Background: Infections are one of the most frequent complications in kidney transplant recipients (KTR). Immunosuppressive drugs represent a strong risk factor for onset of infective diseases. Moreover, also common infections could assume a life-threatening course in KTR. Despite of this, immunosuppression couldn't be discontinued but should be modulated to prevent rejection and, at the same time, to restore an adequate host response. In this point of view, prompt diagnosis and targeted treatment are key points for both graft and patient surviving.

Methods: We report the case of male patient, aged 73 years, with history of recent kidney transplantation in immunosuppressive therapy (steroid, tacrolimus FK, mycofenolic acid), type 2 diabetes mellitus, ischemic cardiopathy with previous revascularization and obliterative arteriopathy of the lower limbs complicated by ulcers. He was hospitalized due to the onset of fever and clinical signs of sepsis caused by ulcer infection. Samples for cultural examinations were collected and antibiotic therapy was started, initially broad-spectrum and subsequently targeted. At the same time, diagnostic imaging tests were performed and the diagnosis of gas gangrene of left foot resulted. The amputation of left lower limb was the choice therapy. Considering the severity of clinical features with poor response to the medications and the worsening of graft function, we decided to start CytoSorb therapy waiting for the amputation. We performed two consecutive CytoSorb treatments (duration: 11 hours and 21 hours, respectively) before intervention and one treatment early after (duration: 24 hours). The cartridge was installed into the Diapact machine (B Braun) with a flow ranging from 120 to 150 ml/min and continuous heparin infusion (600–1000 UI/h).

Results: We observed an improvement in clinical conditions after the first two treatments (defervescence, reduction in inflammation/infection markers) with a complete restoring of diuresis and graft function after the third one. Moreover, we observed a stability of FK blood levels.

Conclusions: In our experience, hemoperfusion with CytoSorb in KTR is safe, doesn't implicate modifications of blood immunosuppressive therapy and has proved effective in limiting septic response in such a complex patient. Moreover, the application of CytoSorb before eradicative intervention could contribute to limit the spread of sepsis, saving the patient.

P08

Successful Treatment with CytoSorb in Two Patients with Septic Shock: A Single Centre Experience

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Background: Septic shock, a life-threatening organ dysfunction caused by a dysregulated host response to infection, is a lethal condition that causes mortality among critically ill patients. The excessive release of inflammatory mediators typically occurs in septic shock and cytokine reduction by hemadsorption represents a strategy for blood purification, developed to attenuate the overwhelming systemic levels of inflammatory mediators. The CytoSorb whole blood adsorber is a device largely used in clinical situations in which inflammatory markers are elevated. In these case series, we evaluated the impact of CytoSorb, used as adjunctive therapy, on hemodynamic and clinical conditions in two patients with septic shock in need of renal replacement therapy.

Methods:

Case 1. A 75-years-old woman, with an history of recurrent cystitis, was admitted to our ICU with septic shock, resulted from a Urinary Tract Infection. At the arrival, mechanical ventilation and antibiotic (Zerbaxa and Gentamicin) and vasopressor therapy were immediately started. Later, the decision was made to install CytoSorb adsorber into the CRRT circuit (Prismaflex, Baxter) to control the progressive shooting of the inflammatory response within 24 h from septic shock diagnosis. The patient received two consecutive CytoSorb treatments: they lasted respectively 8 h and

11 h, because of early coagulation of the extracorporeal circuit. During the treatment, we observed progressive hemodynamic and metabolic stabilization, as a result of increasing control in cytokines storm. There was a reduction in norepinephrine dosage (from >0.2 to 0.15 γ/kg/min), a marked decrease of PCT (from 51.1 to 12.9 ng/ml), PCR (from 43.8 to 30 mg/dl), lactate levels (3.74 to 1.79 mmol/l) and an improvement in renal function, supported by CRRT also. After CytoSorb therapy, we performed two Toraymyxin treatments (2 hours-long each one, for 2 consecutive days).

Case 2. Here is the case of a female patient aged 79-years, who was admitted to our ICU with septic shock due to infected cellulitis on the left leg (Fournier's gangrene). CytoSorb adsorber was installed into the CRRT circuit (Prismaflex, Baxter) within 24 h from septic shock diagnosis. We performed two consecutive CytoSorb treatments, 24 hours-long both, and we continued drug therapy with tigecycline, daptomycin, levofloxacin and norepinephrine. During CytoSorb treatment we observed hemodynamic and metabolic stabilization, associated with an important decrease in PCT (from 87.5 to 12.1 ng/dl) and PCR (from 46.45 to 30.71 mg/dl) concentrations and an improvement in renal function (creatinine values from 2.9 to 0.83 mg/dl).

Discussion: In this work, two patients with septic shock from different causes were effectively treated within 24 h since the diagnosis and achieved hemodynamic and metabolic stabilization. In our opinion, the use of CytoSorb in combination with other supportive therapies (CRRT, Toraymyxin) was beneficial for patients suffering from an overshooting inflammatory response, thanks to its ability to attenuate inflammatory mediators' production. Cytosorb application in both patients affected by septic shock with different types of infection, allowed a restoration of hemodynamic and metabolic equilibrium.

P09

Cytosorb™ and Treatment of Resistant Hemodynamic Shock in a Case of Multifactorial Cytokine Storm

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Background: The Cytosorb™ cartridge contains an adsorbent filter capable of modulating the cytokines which characterize many pathological states; the principal applications of Cytosorb™ are found in sepsis and septic shock. The experience in the use of Cytosorb™ in cases of pathological systemic inflammation is limited in the absence of infection. We report herein a complex case

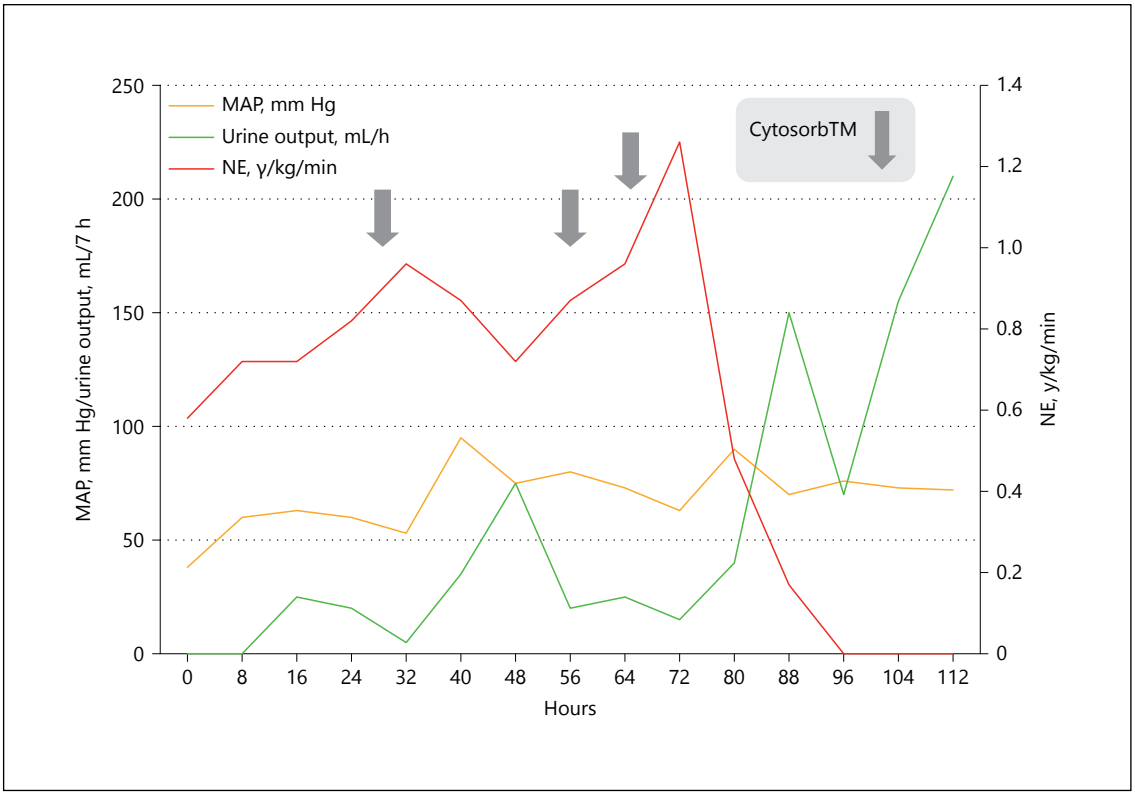

Fig. 1. Trends in mean arterial pressure (MAP), norepinephrine administered dose (NE) and urine output before and after Cytosorb™ treatment. Grey arrow indicates replacement of Cytosorb™ cartridge (for Abstract no P09).

of pathological systemic inflammation (Systemic Inflammatory Response Syndrome – SIRS) in an immunosuppressed patient affected by rheumatoid arthritis (RA) who was treated with Cytosorb™ hemoadsorption.

Methods: The patient was a 64-year-old woman affected by RA treated with methotrexate and anti-TNF-alpha antibodies (Infliximab). She presented to the emergency department with fever, hypotension and hematuria. Laboratory exams revealed: urea 61 mg/dl, creatinine 1.53 mg/dl, pH 7.42, HCO3 20 mmol/l, lactate 14.1 mg/dl, hemoglobin 9.5 g/dl, C-reactive protein 306 mg/L, WBC 11.510/mcL. Abdominal CT and cystography demonstrated a lesion of the bladder wall; bilateral ureteral stents were placed. She was treated with fluid infusions, inotropes, empiric antibiotic therapy with piperacillin/tazobactam and metronidizole, without significant improvement of hemodynamic or laboratory parameters. For the persistence of renal insufficiency and hypotension in the apparent absence of infection (negative urine culture), we initiated continuous renal replacement therapy (CRRT) in the form of venovenous hemofiltration (CVVH) associated with hemadsorption with the Cytosorb™ filter. CVVH was performed in pre-dilution, using heparin 500–750 UI/h anticoagulation. Due to recurrent coagulation of the circuit the Cytosorb™ filter was replaced three times, and thus the total duration of adsorption was about 40 hours.

Results: After beginning the adsorptive and dialytic treatment we observed a progressive improvement of the hemodynamic condition and an increase of the hourly urine output which allowed for the reduction and eventual discontinuation of the noradrenaline (NE) dose (Fig. 1). The patient was transferred from the intensive care unit four days following the end of the Cytosorb™ treatment.

Conclusions: This report describes the application of Cytosorb™ in a complex case of SIRS of unknown origin in a patient with underlying autoimmune disease, immunosuppression and lesion of the bladder wall. Given the clear clinical response after treatment with the CVVH/Cytosorb™ treatment, we hypothesize that the immunomodulation produced by cytokine adsorption allowed a rapid restoration of cytokine and hemodynamic equilibrium. Thus, Cytosorb™ constitutes a useful technique in the management of SIRS, also when the clinical picture is not apparently explained by infection.

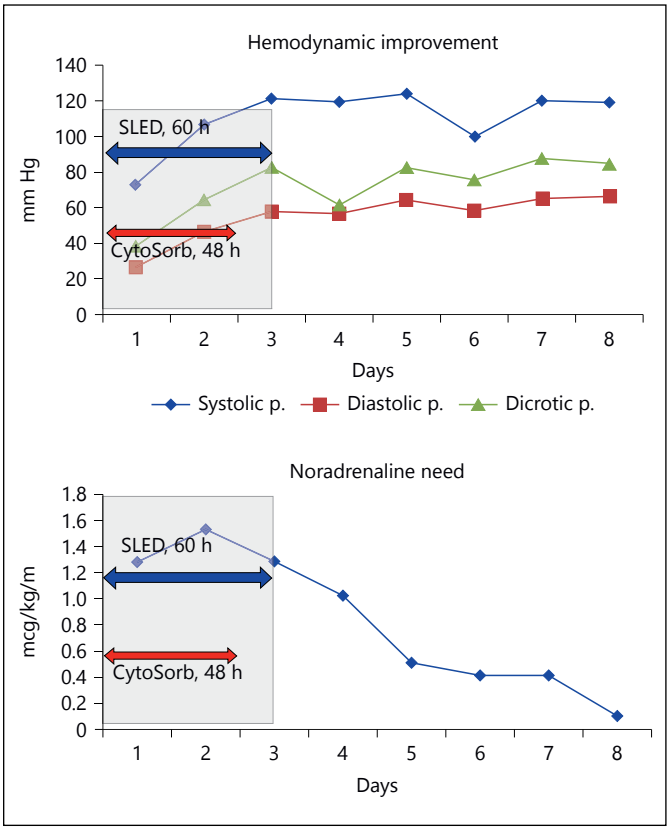

Fig. 1. Hemodynamic improvement during the course of the treatment (for Abstract no P10).

P10

Combined Application of CytoSorb and Sustained Low Efficiency Dialysis (SLED) in a Patient with Septic Shock

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Background: Sepsis is a severe clinical condition, which could lead to Multi Organ Disfunction Syndrome (MODS) and septic shock, associated with high mortality [1]. Acute Kidney Injury (AKI) is a recurring complication in these patients, frequently requiring RRT [2]. CytoSorb hemoadsorption therapy has proved to control the overshooting inflammatory response and the septic condition as a potential immunotherapy.

We report the case of a woman in septic shock and AKI who was treated with CytoSorb in combination with Sustained Low Efficiency Dialysis (SLED).

Materials and Methods: A 50-year-old female reached the emergency room with fever and right hip pain. Medical history showed high blood pressure in pharmacological treatment and frequent urinary infections. Abdominal ultrasound highlighted right kidney pyelectasis, hence the patient was treated by the endoscopic insertion of a ureteric stent, with the emission of purulent urine. During the following hours the clinical picture got worse, with the onset of hypotension, acute respiratory failure, renal failure and the increase of both inflammatory and hepatic cytolysis markers.

Then the patient was admitted to the ICU because of the onset of septic shock: Simplified Acute Physiology Score (SAPS) II and Sequential Organ Failure Assessment (SOFA) Score values were, respectively, 85 and 16, both corresponding to a predicted mortality equal to 90%.

Antibiotic therapy with ciprofloxacin and amikacin was commenced while awaiting results of cultures (blood, urine). After 48 hours the presence of E. Coli was confirmed in the urine culture and antibiotic therapy was consequently changed to meropenem.

Standard therapy was initiated supplemented by the application of life support therapies: fluid resuscitation with crystalloid solution, vasopressors, renal replacement therapy, and early enteral nutrition through nasogastric tube. The patient required high dosages of norepinephrine (1.2 μg/kg/min) and showed elevated procalcitonin levels (40 ng/ml). SLED (Genius, Fresenius Medical Care, Qb: 125 ml/min) in combination with CytoSorb hemoadsorption started for two 24 h-long sessions, followed by a 12 h-long session of only SLED.

Results: Catecholamine dosages could be reduced significantly during the course of the combined treatment accompanied by a clear improvement in the patient's hemodynamic parameters, showing an increase in blood pressure levels and in systemic vascular resistance (Fig. 1). After initiation of specific antibiotic therapy in combination with CytoSorb and SLED, the values of PCT, WBC, CRP, bilirubin and substantially decreased and returned to normal.

Conclusions: The combined use of CytoSorb and SLED proved efficient with regard to hemodynamic stabilization, reduction in inflammatory parameters and recovery of renal function. The literature describes the use of Cytosorb with CRRT [3] and more data are needed to confirm our result about combined use of SLED and CytoSorb in the septic shock and AKI.

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P11

The Use of Cytosorb Therapy in a Patient with Gangrenous Cholecystitis Septic Shock: A Case Report

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Background: Dysregulated systemic inflammatory response in septic shock often results in overwhelming cytokine storm evolving into fulminant sepsis, with multiple organ dysfunction and early death. Extracorporeal cytokine adsorption with the CytoSorb cartridge in addition to regular therapy is a new treatment that could help in managing septic shock patients and reaching shock reversal.

Methods: The following report describes the case of a 63-year-old female patient who was admitted to our Intensive Care Unit with the diagnosis of septic shock. Prior to admission, the patient suffered from severe fever (39°C) in the previous days, frequent emesis accompanied by abdominal discomfort and diarrhoea. Immediately at the arrival, the patient was intubated and mechanical ventilation was started. Chest X-Ray was performed and revealed left pulmonary consolidation, whereas clinical examination allowed the diagnosis of right breast mastitis. Faced with this clinical picture, inotropic support and antibiotic therapy with Meropenem, Colistin, Rifampicin and Daptomycin were started and surgical debridement of breast wound was carried out. Traditional therapy for septic shock led to shock reversal and improvement of the patient's general condition. A few days later, high fever showed up and the markers of sepsis resulted elevated also. A new diagnosis of septic shock was made, this time related to gangrenous cholecystitis. Extracorporeal cytokine adsorption with CytoSorb was then initiated in order to support regular therapy and modulate uncontrolled inflammatory response. The adsorptive column was installed into the Diapact (B Braun) machine and used in hemoperfusion mode, since there was no need of renal replacement therapy. Heparin was administered to reach the correct anticoagulation and blow flow was set at 150 ml/min. After 11.5 hours, femoral catheter dislocation caused an important bleeding, which forced us to interrupt the treatment.

Results: Despite this complication, that was not related to the extracorporeal therapy, the patient's clinical picture noticeably improved. We can report the reduction of inotropic drugs dosage during CytoSorb treatment, but we had to increase the dose again because of the catheter-related bleeding. In general, we obtained shock reversal (reduction in CRP levels, disappearance of fever) and the patient was operated in stable clinical conditions with a subsequent totally recovering.

Conclusions: In this case of gangrenous cholecystitis sepsis applying all traditional therapeutic interventions and CytoSorb as adjunctive therapy resulted in rapid improvement in the hemodynamic situation and resolution of the septic shock condition. CytoSorb along with standard of care therefore appears to be a promising therapy in critically ill patients by facilitating expeditious recovery from the hyperinflammatory state, resurrecting organ function and preventing sequential organ failure.

P12

A Case of Septic Shock with Oliguric Acute Renal Failure Resolved with Cvvhf Coupled with Cytosorb®

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Introduction: Immunosuppression of the transplanted patient makes sepsis the most fearful condition for the survival of both graft and patient. Moreover, the immunosuppressive therapy, although necessary to avert rejection, is able to induce downregulation of the immune system exposing the patient to several pathogens as well. Sepsis is characterized by systemic inflammatory response to injurious events performed by infectious agents. The passage of bacterial, mycotic or viral toxins into the circula-

Table 1. Course of serum procalcitonin and C-reactive protein levels, endotoxinemia, blood count, renal and liver function tests during the ICU stay (for Abstract no P12)

Parameter	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Hb (g/dl)	11.1	10.8	9.7	9.6	9.8	9.7	9.3	10.6
RBC (10^6/ml)	4.3	4.06	3.72	3.74	3.75	3.66	3.68	4.26
Hct (%)	35.1	32.2	29.5	29.6	29.7	29.3	29.4	31.6
PLT (10^6/ml)	120	132	117	120	128	114	106	106
WBC (10^3/ml)	5	7.5	5.7	5.7	6.9	7.7	9.6	18.2
Azotemia (mg/dl)	91	124	156	199	234	236	311	219
Creatinine (mg/dL)	1.95	2.3	2.8	3.3	3.4	3.4	3.8	2.8
Albumin (g/dl)	2.71	2.7	2.1	1.7	2.2	1.9	2.3	2.3
PT (%)	95	84	105		100	86	86	62
PTT (s)	30.6	46.7	29.9	29.8	27.9	30.1	30	43.5
Fbg (mg/dl)	670	502	517	366		174	161	142
Ddimeri (μg/ml)			3,755	4,486		2,370	2,416	3,318
ATIII (%)			80	60		81	77	78
AST (U/L)	39				24		15	13
ALT (U/L)	19				21		13	11
GGT (U/L)	15				56		45	
Total Bilirubin (mg/dl)	0.4	0.4			0.4		0.6	
CPK (U/L)	482	654			63			28
Myoglobin		1,047			112			249
CRP (mg/dl)	16.86	18.6	17.14		5.46	3.4	2.95	
PCT (ng/ml)			1.49	1.05	0.701		0.292	0.128
EAA				0.76			0.75	0.41

tion causes activation of cellular immunity, complement and coagulation cascade against the endothelium. The latter is stimulated by proinflammatory cytokines to produce vasoactive agents with paracrine and systemic effect, involving all the organs and systems (Multiorgan Failure). Thus the mortality is directly correlated to the number of insufficient organs at the same time. The onset of oliguric acute renal failure in patients with septic shock, already initiated to mechanical ventilation, often necessitates the use of extracorporeal with adsorption treatments for the removal of pro-inflammatory cytokines and/or infectious components from whole blood targeting the remodulation of the immune response.

Case: A 72 years old man with double renal transplantation in treatment with TACROLIMUS and MYCOPHENOLATE, was hospitalized for sepsis of the urinary tract and multiple bronchopneumonitis. Despite the rapid onset of a course with LEVOFLOXACIN (500 mg/day) and MEROPENEM 2 g/day (intravenous) and the suspension of immunosuppressive therapy, the patient was transferred to intensive care for respiratory distress necessitating mechanical ventilation and vasopressor support (NORADRENALINE 0.5 mcg/kg/min) to ensure hemodynamic stability. Moreover fluid resuscitation with crystalloids/colloids was performed. Due to oligoanuric renal failure, it was necessary to start CVVHF replacement treatment coupled with a Cytosorb® emulsion filter and citrate anticoagulation. Three consecutive treatments with Cytosorb® lasting 6 hours each every 24 hours were performed. During the intervals the patient continued CVVHF; endotoxinemia, serum procalcitonin and C-reactive protein levels, blood count, renal and liver function tests, serum electrolytes were measured as well as blood pressure, heart rate and oxygen saturation. LINEZOLID 1.2 g/day was added due to the positive blood culture for *Staphylococcus capitis*. The above mentioned approach induced a progressive reduction of procalcitonin (from 1.49 to 0.128 ng/ml) C-reactive protein (from 18.6 to 2.95 mg/dl) and endotoxinemia (from 0.76 to 0.41) mostly after the strengthening of antibiotic therapy. Under a haemodynamical and instrumental point of view we recorded the improvement of blood pressure control (from 105/5 to 144/68 mm Hg) with gradual fading of vasopressors and the reduction of bronchopneumonitis as well.

Conclusions: The case presented demonstrates that treatment with Cytosorb®, coupled with appropriate supportive and antibiotic therapies, can play a significant role in terms of hemodynamics and improvement of inflammation indices in patients with septic shock and acute kidney failure.

Cardiac Surgery and ECMO

P13

Inflammatory Modulation During Heart Surgery: Study Protocol for Randomized Trial

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Background/Aims: Chronic kidney disease (CKD) has consistently been found to be an independent risk factor for the development of cardiovascular disease, increasing the risk of mortality in patients undergoing cardiac surgery. An elevated plasma IL-6 level is commonly observed in CKD patients, which is largely caused by the increased generation resulting from oxidative stress, chronic inflammation and fluid overload. Elevated postoperative plasma concentrations of inflammatory cytokines are associated with an increased mortality and morbidity and plasma IL-6 and IL-10 concentrations predict long-term mortality in adults after cardiac surgery. A novel extracorporeal sorbent haemoadsorption (HA) device (CytoSorb®) was recently developed for cytokine removal from the blood and is now approved in the European Union.

In this pilot trial we aim to assess if intraoperative haemoadsorption with CytoSorb® can significantly reduce postoperative IL-6 serum levels in patients with CKD undergoing on-pump cardiac surgery.

Methods: This will be a single-centre randomised, two-arm, patient-blinded trial of the effects of intraoperative HA on postoperative inflammatory response and organ dysfunction in patients with chronic kidney disease undergoing on-pump cardiac surgery.

Subjects will be randomly allocated to receive either intraoperative HA during cardiopulmonary bypass (CPB) or standard CPB without HA. The HA device will be included in the CPB circuit between the oxygenator and the venous reservoir. The study will be conducted at University Hospital of Catanzaro (Italy).

The primary outcome is the difference in mean IL-6 serum levels between the two study groups on admission to the ICU.

Conclusions: we would like to demonstrate the efficacy of intra-operative haemoadsorption with CytoSorb® to remove cytokines from circulation for prevention of surgical associated inflammatory response and complications in patients with CKD.

P14

CYTOSORB® Membrane May Improve Hemodynamic and the Pro Inflammatory Response in Cardiac Surgical Patients with Pre Operative MOF

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Introduction: CYTOSORB® may adsorbe inflammatory mediators in septic patients, but data on cardiac surgical patients are inconclusive. Aim of this study is to evaluate in cardiac surgery patients with pre operative MOF and cytokine storm: 1) The change of the inflammatory mediators, 2) the haemodynamic response, 3) the changes in organ dysfunction after CYTOSORB® hemoperfusion in the peri operatory period.

Methods: From our local data base, 5 cardiac surgery patients with pre operative MOF were enrolled in the study. All patients were in cardiogenic shock before the intervention (3 Aneurism of AA, 1 endocarditits, 1 mitral regurgitation). In all the patients the Cytosorb cartdrige (Cytosorb Europe GmbH Berlin Germany) was integrated in the extra corporeal membrane oxygenation circuit.

All patients had monitoring of the cardiorespiratory function and evaluation of IL6, IL 10, procalcitonin at basal time -before the surgical intervention -(T0) at 24 hours (T1) and 36 hours (T2) in the post operative period. SOFA score was evaluated at T0 and T2.

All data are expressed as Mean ± SD. ANOVA test was used to compare the changes during time course.

Results: 5 cardiac surgery patients with pre – operative MOF (APACHE II 28 ± 2, SOFA 13 ± 2) were enrolled in the study. All the patients survived to the cardiac surgery operation. IL6, IL 10 ($p < 0.05$) and Procalcitonin ($p < 0.05$) decreased during the peri operative period. SOFA score decreased from 13 ± 2 to 10 ± 6 ($p < 0.01$) with the decreasing of inotropic support.

Conclusions: In cardiac surgery patients with preoperative MOF and cytokines storm CYTOSORB® membrane integrated in the CPB circuite may be useful to improve the organ failures and the cardiovascular function.

P15

First Successful Application of Cytosorb in a Patient Undergoing Transcatheter Aortic Valve-in-Valve Replacement During ECMO

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Background: Extracorporeal blood purification is a modern medical direction based on the modification of blood components outside the patient's body aiming to change their properties or remove pathological substances that cause or support the disease. The use of these methods concerning the pathophysiological pro-

Table 1. Trend of main EGA parameters and sepsis biomarkers from admission to discharge (for Abstract no P15)

	Admission	Before treatment	After 48 h	After treatment	Discharge
pH	7.07	7.36	7.44	7.38	7.45
pO2 (mm Hg)	78	155	156	119	71
pCO2 (mm Hg)	71	34	40	36	40
Lac (mmol/L)	4.8	6.5	1.3	3.6	2.2
HCO30 (mmol/L)	20.6	19.2	27.2	21.3	27.8
IL-6 (mg/dl)	5.2	3.2	2.7	1	0.8
IL-10 (mg/dl)	3.5	7.3	9.5	15.3	26.3
PCT (μg/l)	10.4	9.87	6.56	5.03	2.5
EAA	2.9	2.1	0.9	0.6	0.4
WBC (x10^3/ml)	38.45	32	23.46	12.57	14.49
FE%	20	15		35	48
FAC	18	20		33	38
EoA	0.7	0.6		1.2	1.3

cess allows us to achieve therapeutic effects, even when traditional methods are ineffective.

Methods: We report the case of a 34-year-old male patient who was admitted to the Cardiac Surgery Department at San Carlo Hospital (Potenza, Italy) with heart failure after biological aortic prothesis degeneration and left ventricular dysfunction. Further medical history included aortic valve endocarditis followed by valve replacement with biological prothesis in 2010 and enterococcus faecalis infective endocarditis on the bioprosthetic aortic valve in 2014. In 2018 the patient was admitted to the Cardiac Intensive Care because of pulmonitis. Then the clinical picture worsened due to heart failure, pulmonary edema and fever. Transthoracic and Transesophageal Echocardiogram showed left ventricle dilation, increased wall thickness, reduced ejection fraction (20%) and degeneration, calcification and stenosis (mean pressure gradient = 40–45 mm Hg) of the bioprosthetic aortic valve. High inotropic support and mechanical ventilation were started. Furthermore, blood culture, PCT, endotoxin and IL-6 tests were performed when body temperature rose to 39.2°. After 6-hours-long maximun drug therapy and mechanical ventilation, haemodinamyc instability persisted and worsened gas exchange and oliguria occured. The EGA confirmed clinical deterioration, therefore VA ECMO was implanted with right femoral vein cannulation and right axillary artery side graft cannulation. Initial flow was 2.4 lpm. Since main markers of inflammation were high (Table 1) the decision was made to install CytoSorb cartridge into the ECMO circuit, in order to modulate inflammatory response in view of transfemoral aortic valve replacement. After the first 24 hours of CytoSorb treatment, the patient underwent transfemoral aortic valve-in-valve implantantion in the Cath Laboratory and then was transferred to the Intensive Care. CytoSorb therapy lasted 72 hours and was combined with IGM administration (Pentaglobin 250 mg/kg for 5 days).

Results: Impressive improvement of clinical picture showed, so the patient was weaned from ECMO on the 4 postoperative day. Subsequently, weaning from mechanical ventilation and inotropic support was performed. The patient was discharged on the 21 postoperative day.

Conclusions: This case report proved the efficacy of CytoSorb hemoadsorption combined with ECMO in a patient with heart failure, overshooting inflammatory response and positive blood culture. The sepsis-like sindrome contributed, in our opinion, to the worsening of cardiovascular picture according to septic myocardial failure.

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P16

CytoSorb® in ECMO System and IABP as a Bridge to Reparative Surgery in Ventricular Septal Defect Complicating Acute Myocardial Infarction: A Case Report

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Background: Post-infarction ventricular septal defect (VSD) is a rare but potentially fatal complication of acute myocardial infarction. Definitive cardiac surgery remains the treatment of choice but the operative risk remains high and the optimal timing for surgery is still under debate. Aortic counterpulsation (IABP) and extracorporeal membrane oxygenation (ECMO) represent standards of therapy as a bridge to surgery. We report the use of extracorporeal blood purification therapy (CytoSorb®) after re-

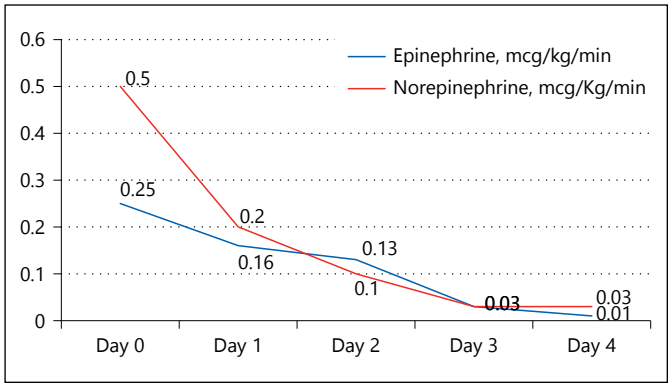

Fig. 1. Inotrope and vasopressor reduction after blood purification therapy (for Abstract no P16).

moval of the ECMO system and after surgical repair of the VSD in a young female patient with severe hemodynamic instability after surgical repair.

Methods and Results: The patient was a 47-years-old Caucasian female (125 Kg, 168 cm) with no previous medical history and a diagnosis of ventricular septal defect as a complication of acute myocardial infarction. The patient needed IABP support and ECMO for severe hemodynamic instability, continuous renal replacement therapy (CRRT) was started for acute renal failure. Surgical repair with a Dacron patch and removal of the ECMO system were scheduled after 20 days of circulatory support. Subsequently, the authors observed persistent severe hemodynamic instability with the need for high dose support with epinephrine (0.25 mcg/Kg/min) and norepinephrine (0.5 mcg/Kg/min). In the absence of hemodynamic improvement extracorporeal blood purification therapy (CytoSorb®) was started for a 24 hours period. The authors observed an immediate improvement in hemodynamics; inotropic therapy could be rapidly reduced and stopped after 5 days. No other complications occurred and echocardiographic follow-up demonstrated nearly normal left ventricular function without residual shunts. The IABP could be removed 4 days after surgery and the patient was finally dismissed after 51 days of hospital stay.

Conclusion: The extracorporeal blood purification therapy (Cytosorb®) appeared as a promising therapeutic option in patients with severe hemodynamic instability and the need of high dose inotropic support.

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P17

Successful Treatment of Postcardiotomy Septic Shock with Venoarterial ECMO and Cytokine Hemoadsorption with CytoSorb™. A Case Report

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Background: Mortality due to septic shock is very high, particularly in patients with heart failure or septic myocardiopathy. In this case VA-ECMO could be useful to prevent irreversible organ damage, however, lack of control of a dysregulated immune reaction may compromise survival. Association of VA-ECMO and cytokine hemoadsorption could be effective in this context.

Methods: A 59-year-old male patient, admitted 20 days after inferolateral AMI complicated by cardiac arrest, underwent off-pump myocardial revascularization. Ejection fraction was 35%, therefore IABP and Swan-Ganz catheter were placed. IABP was removed on third POD, and weaning from dobutamine and mechanical ventilation were started. Hyperthermia and arterial hypotension with no modification of cardiac index (CI) showed at that moment. Nor-adrenaline and adrenaline i.v. infusions were initiated after fluid challenge (T0). Despite CI increase, systemic hypotension worsened and lactate raised (T0+6h). After 12 hours the mean arterial pressure (MAP) was 50 mm Hg although high catecholamine dose, and lactate reached 15 mmol/l. Renal, hepatic and coagulation dysfunctions became evident, and SOFA II score was 15 with 80% expected mortality. PCT, PCR and leucocytes raised too (T0+12h). Peripheral VA-ECMO was established to increase CI and oxygen availability (DO2I), while CVVHDF was started to replace renal function, and CytoSorb™ was installed into the CRRT circuit to prevent cytokine-mediated organ damage, and restore peripheral vasomotor responsiveness. Vancomycin and gentamicin were empirically added.

Results: VA-ECMO increased CI, DO2I, and MAP. The patient's heart contributed to the overall CI (T0+24h). Hemoadsorption, delivered continuously for 3 days, favored rapid clearance of blood lactate, PCT, PCR, and leucocyte count normalization, preserved liver, kidney and coagulation system, and hastened vasoplegia resolution. Adrenaline and noradrenaline were reduced and stopped on 3rd and 6th day of treatment, respectively. CVVDHF was halted in 6th. VA-ECMO was removed on 8th day, when SOFA II score was 8 with 15–20% expected mortality. The patient was weaned from ventilation and dismissed from ICU two weeks later. Blood cultures were negative. Stafilococcus Aureus was isolated from broncoalveolar lavage.

Conclusions: Care of patients in septic shock need to be tailored. In this patient we considered the inability of the heart to increase cardiac output and match increased oxygen requirements, therefore, in front of a quick worsening of SOFA, we implemented VA-ECMO and cytokine hemoadsoption with CytoSorb™. This allowed prompt reversal of the profound vasoplegia and quick removal of catecholamine, hastened clearance of lactate, PCT and PCR, and protected organs already made dysfunctional by sepsis. As matter of facts, SOFA score passed from 15 to 8, and the patient showed a complete recovery.

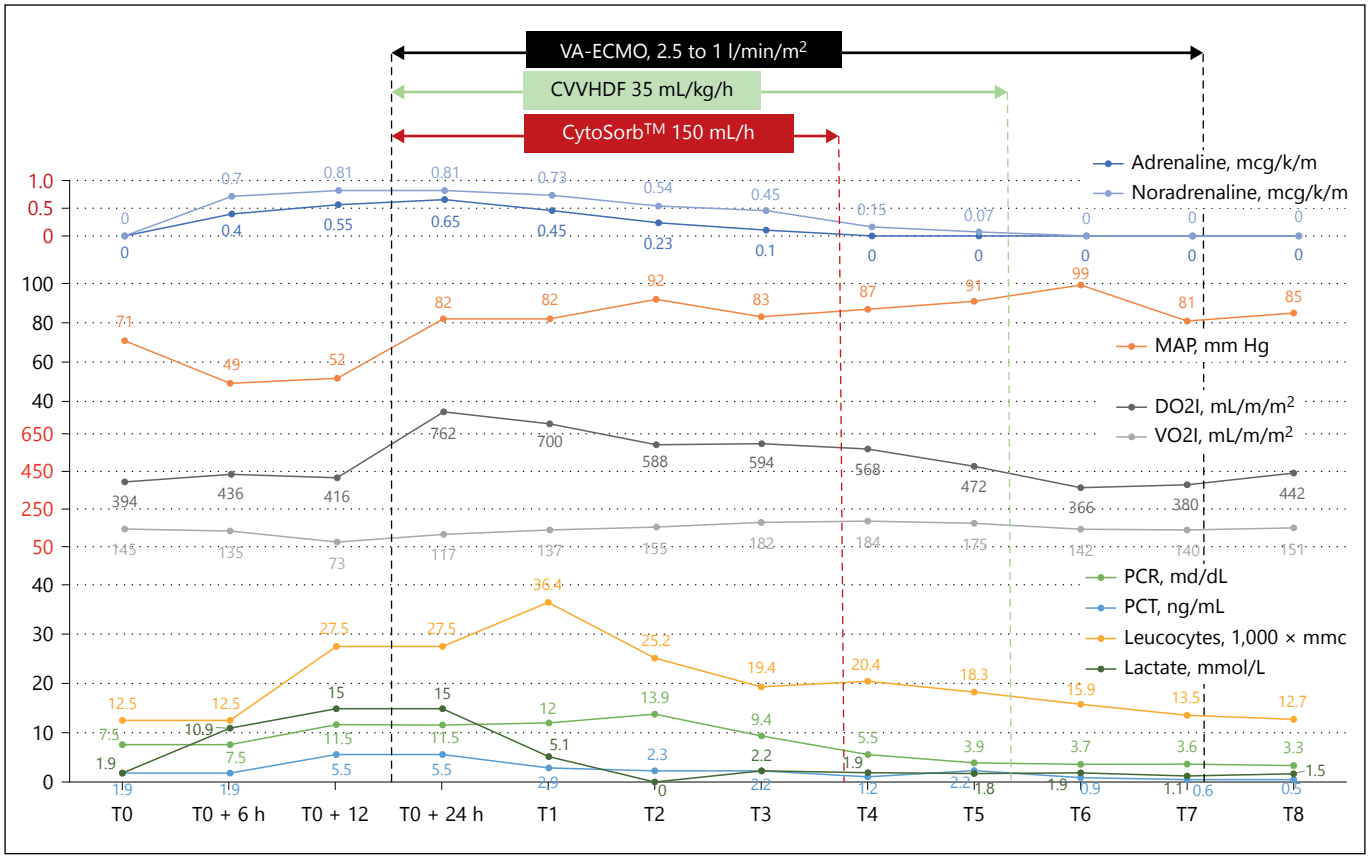

Fig. 1. Trend of cathecolamines, MAP, Oxygen delivery and consumption, inflammatory markers (for Abstract no P17).

P18

Acute Kidney Injury Associated with Infective Endocarditis: Hemoadsorption (Cytosorb® Adsorber) in Combination with CRRT as a Valid Therapeutic Option. A Case Report

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Background: Multiple organ dysfunction syndrome (MODS) associated with septic shock is characterized by high mortality. Current therapeutic guidelines on septic patient management do not support the use of extracorporeal intraoperative cytokine adsorber in patients undergoing cardiac surgery. We report the clinical effects of an extracorporeal therapy performed with the CytoSorb® adsorber in a patient with acute kidney injury (AKI) and septic shock from infective endocarditis.

Case Presentation: A 45-years-old man with a ventriculoperitoneal (VP) shunt due to neonatal hydrocephalus, was hospitalized in Nephrology for septic shock. Blood tests showed a rapid deterioration of renal function (sCr 5 mg/dl, BUN 151 mg/dl), oliguria, anemia, neutrophil leukocytosis and elevated inflammatory markers [C-reactive protein (CRP) and procalcitonin (PCT) were 350 mg/l and PCT 7 ng/ml, respectively]. Endocarditis on mitral and aortic valve was diagnosed (multiple endocarditic vegetations, probable fistulized abscess with pseudo-aneurysm formation and dissection of the mitro-aortic junction). The patient was transferred to Cardiac Surgery Unit to undergo surgery. Due to the presence of persistent arterial hypotension not responsive to fluid therapy and vasopressors, continuous haemodialysis (CRRT: CVVHDF with citrate) was started in association with a 12-hour CytoSorb® hemoperfusion treatment. The extracorporeal cytokine hemoadsorption CytoSorb® is a novel non-pharmacologic technology, able to remove medium-size molecules such as pro-and anti-inflammatory cytokines. CVVHDF has been set on the Fresenius Multifiltrate system. CytoSorb® (CytoSorbents™) was installed in series, downstream to the dialyzer on the same circuit. The patient underwent a double-replacement mitral-aortic valve replacement with a mechanical prosthesis. Subsequently, the patient continued haemodialysis treatment (CVVHDF) associated with a new CytoSorb® cartridge for a further 24 hours period.

Results: The preoperative use of CytoSorb® resulted in a successful reversal of septic shock and a marked improvement in patient's hemodynamic stability in the first 48 hours postoperatively. After the onset of Cytosorb® we observed significantly less vaso-

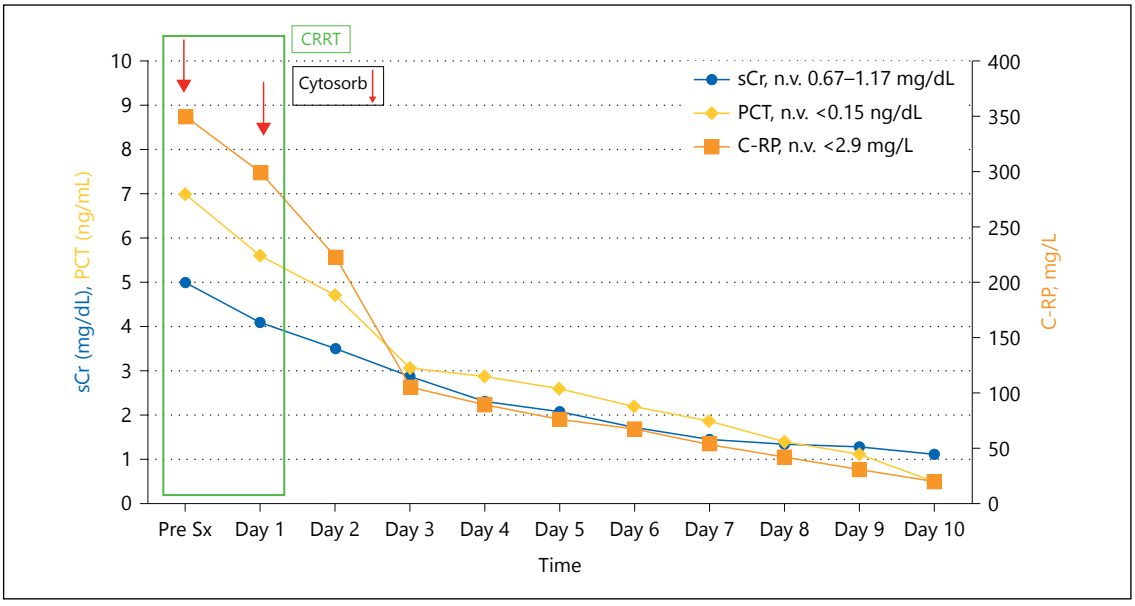

Fig. 1. Course of inflammatory and renal markers (for Abstract no P18).

pressor requirements with a stabilization of the mean values of arterial pressure (MAP). Furthermore, in the following 72 hours a progressive improvement of renal function (sCr 2.89 mg/dl) has been observed, along with the recovery of diuresis and reduction of inflammatory markers (CRP 105 mg/l, PCT 3.05 ng/ml), as shown in Figure 1. The patient was discharged from the Cardiac Surgery Unit after 10 days from surgery with haemodynamic stability and without the need of dialysis therapy.

Discussion and Conclusion: Patients with septic shock are at a remarkably higher risk for developing severe vasoplegia and multiorgan failure. Case reports and case series published recently demonstrated that CytoSorb® treatment in patients with septic shock results in improved hemodynamics, significant decrease in vasopressor dose and effective removal of pro-inflammatory cytokines after 24 hours of application. This case report also highlights the potential effects of CytoSorb® in controlling perioperative vasoplegia, likely modulating postoperative inflammatory response and clinical outcome. In addition, the early use of the CytoSorb® may significantly reduce the need of postoperative renal replacement therapy, favoring a rapid recovery of renal function.

P19

Use of Cytosorb® in Cardiogenic Shock Post Acute Myocardial Infarction with Papillar Muscle Rupture and Severe Mitral Insufficiency: A Case Report

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Background: Despite efforts at early revascularization in acute coronary syndrome and advancing technologies in the field of temporary mechanical circulatory support, the mortality from cardiogenic shock (CS) remains very high (50%) [1]. The systemic inflammatory response, complement activation, release of inflammatory cytokines, (IL-1, IL-6, IL-8, TNF alfa), expression of inducible nitric oxide (NO) synthase (iNOS), and inappropriate vasodilation may play an important role in the genesis of shock and in outcome after [2, 3]. We report on the beneficial application of the device for absorption of cytokines (Cytosorb®) in a patient with CS post Acute Myocardial Infarction (AMI).

Methods: A 62-year-old patient with story of hypertension and diabetes presented with AMI and CS. The circulation was supported by high dose of norephinephrine (0.4 γ/Kg/min), Dobutamine (6 γ/Kg/min), and IABP. The ECG showed an anterior STEMI, CI and PVR were reduced (1.9 and 785 respectively), WP was 21.5. Echo showed a depressed systolic function (35%) and a severe mitral insufficiency due to papillar muscle rupture post AMI. The patient underwent emergency coronary (IVA bypass) and concomitant mitral valve surgery (replacement). After surgery, the patient was treated with cytosorb during CRRT for 24 hours; three

Table 1. (for Abstract no P19)

	Post-surgery	After the first treatment	After the second treatment	After the third treatment
WBC	10.35 x10e/uL	9.86 x10e/uL	8.56 x10e/uL	8.12 x10e/uL
Neutrophilis	85%	82%	83%	80%
Procalcitonin	2.56 ng/ml	3.85 ng/ml	2.24 ng/ml	1.14 ng/ml
Platelets				
PCR	12.55 mg/dl	10.56 mg/dl	8.34 mg/dl	6.12 mg/dl
Norephinephrine	0.25±0.15 γ/Kg/min	0.18±0.12 γ/Kg/min	0.14±0.10 γ/kg/min	0.1±0.12 γ/Kg/min
Lactates	8.5±1.2 mmol/l	6.4±0.7	4.0±1.3	2.3±0.8

treatment were perfomed. We tested WBC, PCR, Procalcitonin and lactates at the end of each treatment.

Results: The levels of norephinephrine after the third treatment were significantly lower then the first (0.25 ± 0.15 vs 0.1 ± 0.12) $P < 0.05$, the lactates after the third treatment were significantly lower then the first (8.5 ± 1.2 vs 2.3 ± 0.8) $P < 0.05$. WBC, PCR and procalcitonin were reduced after the third treatment. CI, PVR and WP improved after the third treatment (2.8, 1250 and 16 mm Hg respectively). The patient was discharged from ICU after 15 days.

Conclusions: lactates levels and the dose of Norephinephrine were significantly reduced after 72 h from surgery. We think that the adsorbtion of cytokines in the CS can reduce norephinephrine levels and improve the tissutal perfusion.

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Drugs Removal

P20

Use of Cytosorb during Cardiopulmonary Bypass in a Patient Underwent Emergent CABG after a Loading Dose of Ticagrelor

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Background: European guidelines suggest dual antiplatelet therapy (DAPT) with acetylsalicylic acid (ASA) and P2Y12 antagonists as standard of care to reduce the risk of thrombotic complications in patients with acute coronary syndrome (ACS). However, this therapy is associated to an increased risk of spontaneous and surgical bleeding, the latter frequently observed when emergent coronary artery bypass grafting (CAGB) is required and ticagrelor or prasugrel are used instead of clopidogrel.

Recent studies show that the intra-operative, on pump, use of Cytosorb might favourably impact on perioperative bleeding, blood product transfusions and re-exploration for bleeding, by removing Ticagrelor from the human blood.

Case Presentation: We report the case of a 83 years old Italian male, suffering from an inferior ST-elevation myocardial infarction (STEMI), unsuitable for percutaneous coronary revascularization. The patient underwent emergent CABG 6 hours after the loading dose of 180 mg of ticagrelor. Given the high risk of bleeding, we decided to implement Cytosorb into the heart-lung machine.

The Internal Mammary Artery (IMA) was anastomosed to the Left Anterior Descending Coronary Artery (LAD), while a Saphenous Vein (GSV) graft to the left marginal artery. Clamping time

was 62', cardiopulmonary bypass time 73', total operation time 270'.

The chest drainage volume after 24 hours was 350 ml, needing 2 packed red blood cell (PRBC) transfusions within 24 h after the surgery. No platelets transfusions have been given. We removed thoracic drainages 3 days after the surgery with 550 ml as total drainage volumes. ICU-stay was 3 days, hospital stay 14 days.

Conclusions: Discontinuation of DAPT is highly recommended whenever possible before open-heart surgery. When not feasible, ticagrelor adsorption with Cyotosorb during CPB may be a therapeutic option.

P21

Severe Quetiapine Voluntary Overdose Successfully Treated with a New Hemoperfusion Sorbent

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Background: Quetiapine is a second-generation antipsychotic drug with clinical efficacy in the treatment of schizophrenia, bipolar disorder, major depressive disorder, and generalized anxiety disorder. Quetiapine overdose, although rare, is mainly linked with tachycardia, QTc-prolongation, somnolence, coma, hyperglycemia, and eventually hepatotoxicity and myocarditis. Extracorporeal techniques for quetiapine removal might be helpful, but only few cases have been reported in literature. In this case report we intended to accelerate quetiapine elimination by applying the hemoadsorbent Cytosorb, able to adsorb hydrophobic substances of molecular weight up to 55 kDa directly from blood, like inflammatory mediators and other endogeneous molecules, such as bilirubin and bile acids. Indeed, CytoSorb has also demonstrated to efficiently remove in vitro some drugs, including quetiapine, thanks to its structure.

Methods: Here, we describe the case of a 27-years-old healthy woman, admitted to our Intensive Care Unit (ICU) after voluntary quetiapine intake and successfully treated with Cytosorb hemoperfusion in combination with CRRT, in order to accelerate quetiapine elimination. The patient, on admission, showed sinus tachycardia and undergone a diuretic therapy with crystalloid hydration, gastrolusis, charcoal and laxative administration. 24 hours after consumption, the quetiapine plasma concentration was 1850 μg/L. Then, we decided to perform hemoperfusion combinated with Cytosorb treatment to reduce the high plasma concentration. We started a Cytosorb treatment in combination with a citrate-based hemodiafiltration treatment CVVHDF for 48 hours, and the cartridge was changed every 24 hours, during which serum quetiapine levels have been measured.

Results: After 12 hours, a good elimination of quetiapine from 1850 μg/L to 648 μg/L has been registered. Later on, an increase of quetiapine in blood concentration has been observed. We decided to continue with another treatment with Cytosorb combinated with CVVHDF. Finally, the patient was extubated 96 hours after the start of hemoperfusion in hemodynamically stable condition and mild tachycardia. She has been discharged to the Semi-Intensive Care Unit after 7 days in a clinically stable condition.

Conclusion: This is the first clinical experience of the potential application of hemoadsorption therapies, as Cytosorb sorbent, in large overdoses of quetiapine. This approach might be feasible to rapidly remove the substance from blood, stabilizing the patient condition. More in vivo experiences are required in order to understand the behavior in the light of the extensive volume of distribution of this substance.

Transplant

P22

Hemoadsorption Perfusion Strategy Mitigates Lung Ischemia Reperfusion Injury Associated to Extended Warm Ischemic Time

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Background: Lungs from donation after cardiac death (DCD) are at risk of unforeseeable extended warm ischemic time (WIT) that in turns may aggravate the severity of lung ischemia reperfusion (IR) injury. Novel hemoadsorption devices may attenuate dysregulated innate immune response associated to lung IR injury. Aims of the current study were: First, to evaluate respiratory mechanics and inflammatory response during EVLP after extended WIT; Second, to evaluate the effect of immune-sorbent therapies on lung IR injury.

Methods: Twenty-two lungs from DCD pigs donors underwent to ex vivo lung perfusion (EVLP) after being randomized to three or six hours of warm ischemic time (3 or 6 WIT). Lungs after 6 hr WIT were further randomized to receive or not Cytosorb during EVLP. All lungs underwent to two hours of reperfusion with blood (10%Hct) to study lung IR injury. Respiraotry mechanics, vascular resistances were calculated hourly over the experimental period. Cytokines concentrations were quantified in perfusate at 1 and 4 hours of EVLP by commercially available ELISA kit. Albumin concentrations was evaluated in lung perfusate at the same time points and in broncoalveolar lavage fluid (BALF) at the end of reperfusion.

Results: See Table 1.

Conclusions: Extended warm ischemic time up to 6 hours is associated with impairment of lung respiratory mechanics during EVLP and more severe IR lung injury after graft reperfusion. Modulation of dysregulated immune response by hemoadsorption strategy attenuates IR-lung injury.

Table 1. Results of the Study (for Abstract no P22)

Variables	Perfusion		p
	Without Cytosorb	With Cytosorb	
During EVLP			
IL1β (pg/ml)	11 (8–14)	10 (9–11)	0.77
IL6	273 (150–281)	39 (29–46)	0.014
IL8	161 (72–228)	83 (78–110)	0.038
IL10	5.6 (3.8–7.2)	2 (1.2–2.5)	0.02
GMCSF	399 (184–362)	142 (86–189)	0.047
After Reperfusion			
$Pplat_{LUNG}$ (%)*			
1 hr	27 (25, 58)	−3 (−18, 14)	0.05
2 hr	18 (13, 42)	−22 (−28, −13)	0.01
$Cstat_{LUNG}$ (%)*			
1 hr	−60 (−70,−52)	−36 (−51, −22)	0.03
2 hr	−55 (−65, −46)	−14 (−28, −4)	0.01
Lung $PI_{ALBUMIN}$	21 (14–28)	12 (7–20)	0.04

* Variable is expressed as percentage change compared to baseline (1 hr after beginning of EVLP).
Pplat, plateau pressure; $Cstat_{LUNG}$, Lung compliance; Lung $PI_{ALBUMIN}$, Lung Permeability Index to Albumin.

P23

Sequential Use of Locoregional Abdominal Perfusion and End-Ischemic Normothermic Machine Perfusion in DCD Grafts with Extremely Prolonged Warm Ischemia Time

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Introduction: Italian law requires 20 min of continuous flat line EKG to declare individual's circulatory death both for controlled (cDCD) and uncontrolled donors (uDCD). Such prolonged warm ischemia time (WIT) forced the introduction of abdominal normothermic regional perfusion (NRP) immediately after death declaration followed by post-procurement ex-situ normothermic perfusion (NMP).

Methods: uDCD suffer out-of hospital cardiac arrest, undergo cardiopulmonary resuscitation and are transported to the hospital under mechanical chest compression. NRP is started immediately after death declaration. Functional (f-WIT) is the time from out of hospital cardiac arrest to the start of NRP. In cDCD f-WIT is the time from systolic blood pressure falling below 50 mm Hg (or oxygen saturation below 70%) to the start of NRP. After procurement grafts are taken to the transplant center and normothermically reperfused.

Results: During the period 01/18–01/19, 15 DCD donors were evaluated. Based on NRP data, 7 (47%) were considered eligible for procurement and ex-situ reperfused. Six (86%) were uDCD donors. One uDCD grafts was discarded during NMP for recipient cardiac arrest at anesthesia induction.

Median donor age was 48 years (range 41–62), median f-WIT 164 min (21–175), median NRP 342 min (294–372), median NMP 188 min (120–360). During NRP median last lactate was 13 mg/dl (0.9–24), median AST peak 290 IU/L (93–691). During NMP median perfusate last lactate was 1.0 (0.6–6.2), median perfusate AST peak 1157 IU/L (604–3164). All grafts except one produced bile, lowest bile pH at 2 hours was 7.37.

No PNF was observed, there were 4 cases (67%) of early graft dysfunction. One patient died for New Delhi metallo-β-lactamase-1 E. coli sepsis. All other post-operative periods were uneventful. No biliary complication was reported.

Conclusion: DCD donation is feasible even with the 20 minutes no touch rule. Strict NRP and NMP selection criteria are needed to optimize post-operative results.

P24

Apheresis in Organ Donation After Cardiac Death (DCD): A Single Centre Experience

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Background/Aims: Organ transplantation is the life-saving treatment for patients with end-stage organ failure. However, the shortage of available organs compared to increasing waiting lists represents a significant problem. To expand the donor pool, selec-

Table 1. Course of organ function parameters and transplantation follow-up (for Abstract no P24)

	CASE 1				CASE 2				CASE 3			
	T0 (15')	T1 (60')	T2 (120')	T4 (180')	T0 (15')	T1 (60')	T2 (120')	T4 (180')	T0 (15')	T1 (60')	T2 (120')	T4 (180')
NRP duration (min)			157				172				219	
Average Blood Flow (ml/min)			4,980				4,580				3,805	
Average Gas Flow (L/min)			4				4.5				4.2	
Average Temperature (°C)			35.6				35.5				36.2	
Average Diuresis (ml/h)			65				80				40	
ALT (U/I)	78	122	162	/	17	/	18	/	43	/	112	121
AST (U/I)	67	107	148	/	25	/	28	/	38	/	51	54
Bilirubin TOT (mg/dl)	0.3	0.28	0.29	/	0.5	0.6	0.7	/	0.64	/	0.6	0.52
Creatinine (mg/dl)	0.75	0.78	0.83	/	0.69	0.72	0.78	/	0.62	/	0.9	0.88
pH	7.426	/	7.338	/	6.935	7.64	7.43	/	7.013	7.387	7.512	7.531
PaO_2 (mm Hg)	52.6	39.4	41.2	/	54.5	36.3	43.2	/	42.6	39.1	39.3	29.3
$PaCO_2$ (mm Hg)	88	36.9	41.3	/	102	23.9	40.8	/	103	42.3	34.6	33
BE (mmol/l)	–9.8	5.5	3.2	/	–10.8	4.9	4.6	/	–5.1	0.3	4.5	4.7
Lactates (mmol/l)	13	6.7	5.8	/	11	8	6.6	/	9.9	4.3	1.5	1.9
ORGANS FOLLOW-UP												
Liver			ALIVE				ALIVE				ALIVE	
Right kidney			ALIVE				ALIVE				ALIVE	
Left kidney			ALIVE				ALIVE				ALIVE	

tion criteria have been extended, including also Donors after Cardiac-Death (DCD). The main problem related to DCD is the extended Warm Ischemia Time and the uncontrolled production of inflammatory molecules, responsible of organ deterioration and Primary Graft Dysfunction (PGF). In-situ Normothermic-Regional-Perfusion (NRP) for abdominal circulation has been used to improve organ conditions and, the addition of CytoSorb, an extracorporeal cytokines adsorber, might be a potential solution to limit organ injuries.

Methods: We report a case series of 3 DCD donors treated with NRP to maintain circulation before organ retrieval, in association with CytoSorb.

Donors were admitted at our ICU as potential Cardiac-Death-Donors (1: post-cardiac arrest polytrauma patient with return of spontaneous circulation; 2: stroke; 3: stroke). After cardiac-death confirmation (20 min), consent for transplantation was given. Patients were transferred to the operation room with venous-arterial NECMO plus CytoSorb (in parallel). During perfusion, biological and metabolic parameters were monitored: lactate, bilirubin, ALT, AST, creatinine, PaO2, PaCO2, pH. NECMO was set at maximum flow rate, according to patient's BSA, to maintain an optimal abdominal organs perfusion and to prevent irreversible organ damage. Average temperature set-point was 37 °C. Liver, kidneys and tissues were procured in all DCD donors in a standard method.

Results: NECMO support began immediately after 20 min (no-touch-period). The treatment duration ranged from 150 to 219 min. During perfusion, lactate levels progressively decreased (average value, from 10.3 mmol/l to 4.7 mmol/l), as sign of improvement in organs perfusion and quality. Parameters describing organs function maintained stable (average values: creatinine 0.77 mg/dl, bilirubin 0.59 mg/dl, haemoglobin 7.2 g/dl). CytoSorb blood flow maintained stable: average flow rate about 10% of NECMO flow. Transplantation outcomes have been positive: organs, during procurement, were judge transplantable and assigned to recipients, according to waiting lists. Six kidneys, three livers and tissues were overall transplanted. During a median of 2 days of stay at ICU, the 3 liver recipients were released after an overall average recovery of 13 days (average values: bilirubin 0.92 mg/dl, AST 30 U/l, ALT 186 U/l, creatinine 0.86 mg/dl, INR 1.07). During follow-up (180–30 gg) no functional decline was seen in the donated organs. All the data are reported in Table 1.

Conclusion: Organ donation from DCD has been widely used in many transplantation centres to expand the organs pool. In these donors, NRP in combination with CytoSorb, an adjunctive therapy to remove inflammatory mediators, responsible of organ deterioration, rejection and PGD, might help to successfully limit irreversible organ damages. 9 major organs (six kidneys, three livers and tissues) were successfully donated. During follow-up all the recipients are still alive.

Liver Failure

P25

Comparative Efficacy Between Two In Vivo Techniques for Bilirubin and Bile Acids Removal

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Background: In both intra and extrahepatic bile stasis a gradual increase of bilirubin and bile acids values occurs, causing symptoms as uncontrolled itch with skin lesions and kidney failure, known as Cholemic Nephrosis [1]. Furthermore, biopsy shows bilirubin accumulation in bile ductus and intracellularly, but bilirubin removal acted by liver is very slow if not impossible. Extracorporeal blood purification showed to be decisive [2] and contributes to the reduction of pre-load pigments which have to be removed from liver. Dialysis systems are completely ineffective for the removal of these molecules, while adsorption by resin and/or carbon columns has revealed to be effective in vitro and in vivo. Since in a previous preliminary study the authors found advantages of adsorption by two resin systems compared to other three methods commercially available, they wanted to deepen the comparison of in vivo efficiency of these purification therapies.

Materials and Methods: Samples were performed in pre and post-adsorbents positions, so that the mass clearance of total and direct bilirubin and bile acids obtained with plasmapheresis and plasma perfusion (CPFA®) was compared with the one obtained with hemoperfusion on Styrene Divinylbenzene column (CytoSorb®). Treatments were carried out with citrate anticoagulation, then hemoperfusion was coupled with CVVH, since the latter was unable by itself to remove bilirubin, in order to avoid the accumulation of citrate.

Results: 37 treatments performed with CPFA and 11 with CytoSorb® were compared. The first ones had an average duration of 8 hours (DS 2.7) after which, as previously reported, the system tends not only to lose effectiveness, but also to release part of the adsorbed bilirubin. This phenomenon has never been detected with CytoSorb®, whose use is recommended for 24 hours. The average duration of treatments with this adsorptive column was 20 hours (DS 5). The results are reported in the table below.

The difference is statistically significant ($p < 0.01$) for both total and direct bilirubin and bile acids, in favour of CytoSorb®. This is valid either for the entire treatment or the first three hours, in both methods characterized by a higher yield.

It can be emphasized how the resin adsorbs both direct and indirect bilirubin, as demonstrated by the stability of direct/total ratio and especially by the fact that the patient's hyperbilirubinemia was predominantly indirect.

Discussion and Conclusions: The removal kinetics showed a progressive performance decrease in both systems, but CytoSorb® demonstrated to have either a greater efficiency, as revealed from the first three hours of treatment (mean total bilirubin removal 546 vs 323 mg and bile acids 723 vs 281 mcMol), or a longer duration. This is the reason why CytoSorb® was able to reach a greater mass clearance of the analysed molecules, making it preferable compared to the other systems available on the market. Also, the simplicity of the technical setting represents an undeniable advantage.

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P26

Blood Purification After Liver Transplantation Could Be a Useful Choice?

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Introduction: It is known how biliary complications are among the most frequent and major sources of morbidity, graft loss, and mortality after liver transplantation and that high bilirubin levels (HBL) and bile salts can cause toxic effects on the brain and induce damage also in other tissues. Many studies have been done about bilirubin neurotoxicity, and it is clear how high levels of this molecule conduct to modifications in synaptic neurotransmission and

Table 1. Results of the comparative study after three hours and the entire treatment (for Abstract no P25)

	Entire treatment			First 3 hours		
	Total Bilirubin (mg)	Directed Bilirubin (mg)	Bile acids (mcMol)	Total Bilirubin (mg)	Directed Bilirubin (mg)	Bile acids (mcMol)
CPFA	531±198	389±161	508±336	323±125	230±89	281±176
CytoSorb	1,860±1,897	1,488±1,756	1,503±1,131	546±475	503±497	723±634

Table 1. UNIvariate and MULTIvariate analysis in relation between BCR and complications (for Abstract no P26)

Logistic regression	Odds Ratio	P>z
BCR24h vs Leakages	13.26	0.02
BCR24h vs ITBL	5.09	0.09
BCR1w vs Mortality 90 days	1.56	0.04
Multivariate Cox-Regression	**Haz. Ratio**	**P>z**
BCR24h vs Mortality 1 year	1.61	0.01

Spearman
PDR vs BCR1w
Test of Ho: BCR1w and PDR are independent
Prob >|t| = 0.0140

change microvascular blood flow. In particular, HBL seem to work as an electron-transport poison on every mammalian cell. In fact, when bilirubin levels raise, cell-death increase. Luckily, albumin bounds bilirubin and the complex is nontoxic to tissues. Also high HBL consequences on the lung are well studied: it impairs the surface tension activity in a dose-dependent manner. Bilirubin and bile salts have effects also on native and transplanted liver, they are lethal to hepatocytes and their accumulation in cholestatic syndrome may affect hepatocellular injury. The mechanism of injury is dependent on ATP depletion, which creates a damage similar to a form of anoxia injury. Intracellular bile salt retention may be a critical mechanism triggering hepatobiliary injury after liver transplantation, due to the potent detergent properties towards cellular membranes of hepatocytes and biliary epithelial cells. Clinically, elevated levels of bile salts and bilirubin are relevant in the genesis of transplantation related complications. And, ischemic-type biliary lesions (ITBL) are a serious complication, able to cause delay graft failure, whose incidence can occur in a range between 5% to 15%.

Our Experience/Aim: We studied how bilirubin could be a risk factor for biliary complications, which are the major cause of morbidity and liver failure after OLT procedure. In particular, we search the positive predictive value of decreased bilirubin clearance ratio in the development of biliary complications, comorbidities and mortality.

Materials and Methods: We investigated all patients undergoing OLT in the hospital of Udine from 2010 to 2018. We excluded, for research-technical reasons, patients without the determination of indocyanine green (ICG-PDR) data and homogeneous features. Data of 77 patients were collected and retrospectively analyzed. Every possible association between each predictive variable and each complication has been studied using Cox-regression method. Then, all variables characterized by positive correlation have been studied using a multivariate Cox-regression model. Kaplan Meier plot was used to estimate the overall survival. Stata software was used version 15. Bilirubin clearance ratio (BCR) at 24 h after OLT was calculated as percentage variation in the first P.O. day and after 7 days.

BCR24h = (bil.value 24 h after OLT – opening post OLT bil. value)/opening post OLT bil.value BCR1w = ((bil.value 7 days after OLT – opening post OLT bil.value)/opening post OLT bil. Value).

Results: UNIvariate and MULTIvariate analysis in relation between BCR and complications are shown in the Table 1.

Conclusions: Decreased bilirubin clearance ratio 24 h post-OLT and one week after OLT are two major predictors of biliary complication such as leakages and mortality. This feature could be explained by toxic damage caused by bilirubin and bile salts on hepatocytes, cholangiocytes and all epithelial cells. This toxicity may be increased by subnormal level of albumin, as a protein able to tamponade the bilirubin toxicity and with anti-inflammatory properties on oxidant stress. In that way, blood purification may be helpful to remove the inflammatory mediators and to restore the immunological patient function.

P27

High Cut-Off Continuous Veno-Venous Hemodialysis Associated with Hemoadsorption Effectively Remove Bilirubin and Contribute to Prevent Hyperbilirubinemia Induced-Acute Kidney Injury. A Single Center Experience

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Introduction: Severe hyperbilirubemia (usually up to 20 mg/dL) is associated with various forms of acute kidney injury (AKI) such as the cholemic nephropathy histologically characterized by the presence of intratubular bile casts and tubular injury. Although the pathogenic effects of bilirubin on renal tubular epithelial cells are incompletely understood, hemodynamic alterations or direct toxic damage have been hypothesized. Recently, it has been demonstrated that bilirubin might induces pro-apoptotic effects on tubular epithelial cells during renal ischemia/reperfusion injury. Indeed, the highest incidence of hyperbilirubinemia induced-AKI has been demonstrated in patients affected by hepatorenal syndrome (HRS) due liver cirrhosis, cardiogenic shock and sepsis.

Aim: The aim of this study was to investigate whether high cut-off continuous veno-venous hemodialysis (HCO-CVVHD) associated with hemoadsorption is able to reduce hyperbilirubinemia preventing hyperbilirubinemia induced-AKI.

Materials and Methods: We retrospectively analyzed the clinical data of six patients affected by hyperbilirubinemia due to cholangiocarcinoma (2 pts), sepsis (2 pts) and liver cirrhosis complicated by HRS (2 pts). Patients were treated with citrate anticoagulated HCO-CVVHD associated with CytoSorb, a hemoadsorber characterized by a highly porous, biocompatible polymer capable of binding a broad spectrum of hydrophobic compounds with a molecular weight between 10 and 55 kDa. HCO-CVVHD was performed with EMiC2, a 1.80 m^2 polysulfone hemofilter with a cut-off at ~30 kD. Blood flow was maintained at 100 mL/min and dialysate flow rate at 33 mL/min.

Results: The mean age of the patients was 69.1 ± 17 yrs. Mean serum creatinine and mean urine output at the start of HCO-CVVHD (T0) were 1.2 ± 0.15 mg/dL and 10 ± 5 mL/h, respectively. Mean serum bilirubin at T0 was 34.35 ± 13.05 mg/dL. The planned duration of HCO-CVVHD was 72 hrs. 1/6 patients deceased during the treatment. Mean serum bilirubin significant decrease already after 48 hrs of treatment (T48) (34.35 ± 13.05 vs 20.55 ± 4.85 mg/dL, $p < 0.01$) together with a significant increase of the urine output after 72 hrs (T72) (10 ± 5 vs 100 ± 26 mL/h, $p < 0.01$).

Conclusions: Our results suggest that high cut-off continuous veno-venous hemodialysis associated with hemoadsorption may contribute to reduce hyperbilirubinemia by a percentage of about 40% allowing a preservation/protection of kidney function.

P28

Successful Treatment of Bilirubin Nephropathy by CytoSorb Hemodialysis

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Background: Anabolic steroids abuse is frequent, as purchasing became easier through online stores. (1) We present the case of a 52-year-old man who took steroids for anabolic use, causing acute liver failure, with development of bilirubin nephropathy. (1) We used CytoSorb cartridge (2), with standard hemodialysis, with satisfyng results.

Case Report: A 52-year-old man, with overall good health, was hospitalized for general discomfort and jaundice.

The clinical history was irrelevant. However, he reported he had taken trenbolone, stanazole and metandrostrelone (unspecified dosage) for anabolic purposes, for approximately two months prior the hospitalization. The baseline bloodtestes showed: bilirubin up to 50 mg/dl, AST/ALT twice the norm, normal GGT and ALP, serum creatinine 3.34 g/dl. Viral, autoimmune and tumor markers were negative.

Abdominal CT and MRCP revealed empty gallbladder, nondilated bile duct. The liver biopsy did not detect cholestatic. The first-line treatment with plasma-perfusion (three sessions with dedicated filters) was unsuccesful. Renal replacement therapy with hemoadsorption was started in order to reduce bilirubin levels, to prevent encephalopathy and to take time so that the liver starts to flow the bilirubin correctly or initiate the patient for a liver-kidney transplant. For this purpose, we used three cycles of CVVHD with hemoadsorption using CytoSorb®. The first cycle of therapy was scheduled for 72 hours with the use of three absorbent CytoSorb. Meanwhile, bilirubin levels were checked frequently, pre and post sorbent, to verify the absorption gradient. The patient developed progressive hypoalbuminemia and hypophosphatemia, which were corrected.

However, the second part of the first cycle was interrupted after 13 hours (instead of 24 h), as the patient was complaining of general discomfort. The first therapeutic cycle was completed within the last 24 hours of dialysis with absorbent. In the following days, three hemodialysis sessions were performed. We then observed the kinetics of bilirubin levels during a three-day interval before the second cycle. The constant raise of bilirubin levels forced to complete the other two additional hemodialysis cycles with sorbent (72 h for cycle, 24 hours between cycles, 7 CytoSorb).

Results: At the end of the three cycles, the bilirubin levels were 11.39 mg/dl, (Table 1) the onset of encephalopathy was avoided, and the patient was correctly initiated to the liver-kidney transplantation procedure.

During the controls to be included in the transplants list, the blood values of bilirubinemia and creatinemia started to go down autonomously, a sign that the liver had correctly resumed secreting bilirubin, thus making transplantation and dialysis unnecessary.

Conclusion: Based on this experience, we recommend the use of CytoSorb with CVVHD in patients with hyperbilirubinemia, in order to prevent complications and to address them to specific therapy or transplantation. For further observations, we recommend to monitor serum electrolytes and albumine in order to reintegrate them.

Table 1. Bloodtests values after treatmant (for Abstract no P28)

Serum value	Starting value	After first cycle of treatmant	After second cycle of treatmant	After thrid cycle of treatmant
Total bilirubin	51.24	22.82	19.94	11.39
Creatinine	11.78	2.6	1.69	2.21
Na+	134	136	137	139
K+	4.45	4.22	3.85	3.62
Mg+	2.58	1.82	1.67	1.67
Phosphorus	4.14	2.97	1.39	1.73
Calcium	9.21	8.32	8.8	8.52
albumin	33	27.7	30.1	26.3
Urea	102	36	9	14

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P29

Bridging to Transplant a Patient with Acute-on-Chronic Hepatic Failure: The Role of CytoSorb Haemoadsorbtion

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Background: CytoSorb is a synthetic extracorporeal haemoperfusion adsorption column, able to remove inflammatory cytokines and among others bilirubin and bile acids, thus supporting impaired liver function as a possible bridge to liver function recovery. We report on a case of acute-on-chronic liver failure, hospitalized in the ICU after gastrointestinal bleeding.

Case Report: A 51-year-old male, with liver cirrhosis due to long lasting HCV-related chronic infection, never evaluated for treatment, was brought to the local Emergency Room due to sopor and left hemiparesis after recurrent episodes of hematemesis and melena. Severe anemia (Hb 4.7 mg/dL) as well as hyperglycaemia were evidenced. Massive haemorrhage protocol was started before a CT scan. He underwent emergent endoscopic treatment for cardial ulcer bleeding; concomitant non-bleeding oesophageal F3 varices were diagnosed. He was admitted to ICU, requiring mechanical ventilation and vasoactive support. His wife reported being unaware of his advanced HCV-related liver disease until the current episode. After ICU hospitalization, control EGDS for persistent and untreatable bleeding and recurring anemization led to positioning of a Sangstaken-Blakemore device, held in place for 10 days. Liver function was severely altered, with ensuing coagulopathy (INR 5.4), hyperbilirubinemia (Zenith 31 mg/dL) and increased creatinine (4.36 mg/dL). The patient was referred to the referent Liver Transplant Center at this stage, but transfer was denied because of neurological impairment, mechanical ventilation and hemodynamic instability. Plasma-exchange treatments were therefore performed daily, with 5% albuminate solutions; continuous haemodialysis was started, in association with the CytoSorb filter. A CytoSorb column was plugged into the CRRT circuit, each session lasting approximately 24 h. The patient received 96 h of CytoSorb therapy in total, over 4 sessions. Bilirubin decreased to 15 mg/dL, creatinine to 0.61 mg/dL. Brain CT scans were persistently negative for ischemic/haemorrhagic lesions, and his consciousness ameliorated, with progressive recovery of his left motor deficit. He was extubated after 18 days, with stabilized haemodynamics; he was discharged to the local Infectious Diseases Unit after 22 d in ICU. After interruption of CRRT hemofiltration& CytoSorb, hyperbilirubinemia worsened up to 28 mg/dL, with creatinine stabilized at 2.1 mg/dL. His MELD score was 32. At this stage, however, due to persistent haemodynamic stability and full neurological recovery, transfer to the Liver Transplant Unit was granted. Three additional cycles of plasma-exchange were performed. The patient was successfully and uneventfully transplanted after 14 d.

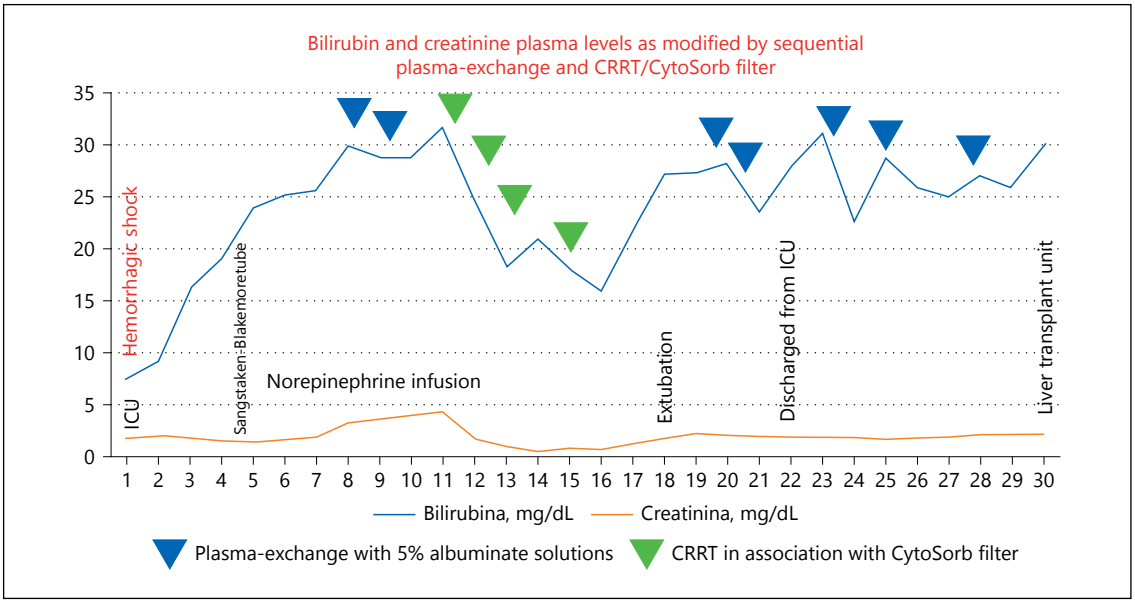

Fig. 1. (for Abstract no P29).

Conclusions: In our patient, with acute on chronic liver failure due to massive digestive haemorrhage, cytokines may well have played a relevant role on persistent, severe impairment of an already hampered organ. The use of CytoSorb may therefore have provided an etiologic, as well as depurative treatment, allowing successful bridging to meet the criteria for eligibility to liver transplantation.

P30

CytoSorb as an Organ Support Therapy During Acute Liver Failure: A Case Report

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Background/Aims: Acute severe hepatic failure associated with persistent hyperbilirubinemia and inflammatory markers increase is a life-threatening critical illness affecting multiple other organs, including renal and cerebral function. Nowadays, extracorporeal techniques for blood purification are largely used in the context of sepsis and septic shock, for cytokines removal, and liver failure, for bilirubin adsorption. CytoSorb is an absorbent device that can be integrated in any extracorporeal circuits and is able to absorb from whole blood inflammatory mediators, bilirubin and other hepatic enzymes. Here we report the case of a patient with Acute Liver Failure and increase inflammatory markers, efficiently treated with CRRT with CytoSorb, as adjuvant therapy for organ support.

Case Presentation: We report a case of a woman with an history of arterial hypertension, type 2 diabetes mellitus, psoriasis, obesity (BMI: 39), moderate CKD (eGFR 45), COPD with OSA in therapy with BiPAP and O_2. In 2017, she underwent left hemicolectomy surgery, following treated with adjuvant chemotherapy for colon cancer. In December 2018, the patient was candidate for right hepatic resection (ALLPS technique), for colorectal liver metastases. After liver surgery, the patient was moved to the ICU. On the fifth postoperative day, we started CRRT (Ci-Ca CVVHDF, Multifiltrate), due to progressive deterioration of kidney function, associated with hemodynamic instability and electrolytes alterations. After a TAC evaluation, the patient needed a second surgery to complete the right hepatic resection and in the next few days a worsening in liver function (increased transaminase, bilirubin and coagulation values and phlogosis indexes was observed. In order to support liver function, by reducing bilirubin and other hepatic molecules, and to modulate the uncontrolled inflammatory response, CytoSorb column was placed in the CRRT circuit (predialyzer position). We performed 4 CytoSorb treatments, 24 hours each.

Results: The combined treatment improved general clinical conditions. We observed a reduction of the SOFA cardiovascular score as compared to baseline (4 vs. 2) after 4 days of CytoSorb treatment, accompanied by a spontaneous stabilization in the following days. Liver function indicators (GOT, GPT, LDH direct and total bilirubin) did not drastically worse as expected and maintained stable during the treatment. Furthermore, a rapid improvement of phlogosis index occurred, accompanied by a stabilization of metabolic and hemogasanalytic parameters and a progressive improvement of kidney function with diuresis recovery.

Conclusions: We present the use of combination therapies in a patient with Acute Liver Failure and uncontrolled inflammatory response. CytoSorb has proved to be an efficient therapy to reduce uncontrolled inflammatory response, thanks to the capability to remove inflammatory mediators from blood, allowing a stabilization of metabolic and hemodynamic parameters (lactates and hemogasanalytic values). CytoSorb also might help to support liver function and its recovery, thanks to the modulation of worsening hyperbilirubinemia, increasing toxic catabolites, hardly removable from blood, and cytolysis enzymes, also allowing a stabilization of coagulation parameters.

Table 1. SOFA cardiovascular score and Laboratory characteristics at baseline and during CytoSorb treatment (for Abstract no P30)

	ICU admission	2nd day	7th day	8th day	8th day	9th day	10th day	11th day	12th day	13th day	16th day
SOFA cardio (mcg/kg/min)	0	3 (0.09)	3 (0.09)	4 (0.16)	4 (0.23)	4 (0.16)	3 (0.06)	3 (0.08)	2 (0.01)	1	0
PCR (mg/dl)	2.49	1.17	27.01	27.27	13.54	12.88	17.8	18.6	15.36	14.11	13.12
PCT (ng/ml)	/	1.7	4.1	4.06	3.06	2.73	2.37	1.86	1.51	1.82	1.60
Lactate (mmol/l)	0.7	0.8	2.8	4.1	6	4.8	3.9	2.5	1.8	1.7	1.5
Diuresis (ml/h)	/	20	100	40	0	5	5	0	30	80	50
Creatinine (mg/dl)	1.08	1.43	2.92	3.53	3.16	2.46	1.85	1.59	1.52	1.33	0.75
eGFR (ml/min/m^2)	49.6	35.3	14.9	11.8	13.5	18.3	25.8	31	32.8	38.5	77.10
GOT (U/L)	70	759	78	66	173	176	147	58	59	61	60
GPT (U/L)	69	655	240	168	115	108	/	/	45	44	52
Bilirubin TOT (mg/dl)	0.74	1.28	2.89	3.22	3.65	4.30	4.03	3.79	4.99	6.82	8.01
Bilirubin DIR (mg/dl)	/	0.65	1.84	2.11	2.36	2.63	2.47	2.12	2.99	4.11	4.70
LDH (U/L)	/	1,659	181	/	522	336	/	/	260	237	245
Ammonium (umol/L)	/	67	52	67	87	61	/	67	57	59	46

P31

ECMO in Combination with CytoSorb in a Woman with Para-Prosthetic Leak Following Mitral Valve Replacement, Candidate to Percutaneous Treatment: A Case Report

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Background/Aims: In patients with complex pictures near to Multi Organ Failure, characterized by cardio-pulmonary failure, that require ECMO support and with kidney and liver function loss, the use of a sorbent cartridge, as Cytosorb, could be a valid support thanks to its capability to adsorb a very large quantity of inflammatory mediators and other molecules, like bilirubin, bile acids and ammonium. Moreover, Cytosorb can be used into any extra-corporeal circuits, as Continuous Renal Replacement therapy (CRRT), Extra-Corporeal Membrane Oxygenation (ECMO), Cardio-Pulmonary Bypass (CPB) or isolated circuits for hemoperfusion, adapting its use to the clinical need.

Case Presentation: We report a case of a woman with a story of aortic coartation and mitral valve dysplasia, subjected to decoartectomy associated with multiple mitral valve substitutions over the years. In 2017, during an echocardiographic control, we found a mitral para-prosthetic leak and severe tricuspid regurgitation, associated with increased haemolysis index, dyspnoea and asthenia. We decided to admitted her to our hospital and to proceed with a percutaneous treatment of paravalvular leak. After the first attempt to repair the mitral valve paravalvular leak, we decided to postpone the procedure, due to a persistent severe mitral regurgitation. On the first postoperative day, the patient underwent VA-ECMO, due to a cardiac arrest followed by return of spontaneous circulation. Thanks to ECMO support, we successfully performed the percutaneous treatment of paravalvular leak and the tricuspid valve substitution. After four days of hospitalization in ICU, during ventilator weaning, tachypnoea associated with ARDS occurred and we implanted VV-ECMO in emergency. After seven days, we started CVVHDF (Prismaflex, Baxter) in association with CytoSorb (in series to the haemofilter), due to the development hyperbilirubinemia associated with hepatorenal syndrome. At the same time, we decided to wean the patient off from VV ECMO therapy.

Results: The application of combined therapies, ECMO, CRRT and Cytosorb, helped restoring the patient general conditions. In a complex setting of severe mitral and tricuspid valve regurgitation associated with mitral para-prosthetic leak, the cardio-pulmonary function was restored; at the same time, ventilatory and metabolic parameters rapidly improved, allowing the achievement of physiological values. $PaCO_2$ and PaO_2 stabilized over time, concomitantly with acid-base and electrolyte normalization. The application of CytoSorb supported the stabilization of bilirubin levels and liver parameters, helping to control the patient continuous release.

Conclusion: We present the use of combination therapies in a patient with a complex clinical picture. ECMO therapy associated to CVVHDF with CytoSorb, has proved to be an efficient method to support cardiac and lungs function and to support the kidney and liver failure. In particular, CytoSorb cartridge seems to be a promising therapy, able to control and modulate worsening hyperbilirubinemia, allowing progressive liver function recovery.

P32

Hemoperfusion with CytoSorb for Bilirubin and Cytokine Removal in a Cardiac Surgery Patient

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Background: Removal of bilirubin through extracorporeal blood purification is an increasingly common technique that supports hepatic detoxification function, especially in critical patients. In this context, the CytoSorb cartridge is able to adsorb cytokines, bilirubin, bile acids and a huge spectrum of other molecules involved in liver dysfunction, aiming to support traditional therapies and facilitate patient's recovery.

Methods: This case reports on a 62-year-old female patient who was admitted to our Cardiac Intensive Care Unit after mitral valve replacement. History highlights mitral valve annuloplasty in 2010, high blood pressure, atrial fibrillation treated with anticoagulant therapy, obstructive sleep apnoea syndrome, obesity and bronchiectasis. After surgery, high fever, leucocytosis and hemodynamic instability showed, so antibiotic and vasoactive therapies were started. Blood culture resulted negative, but Bronchoalveolar Lavage was positive to pseudomonas aeruginosa, therefore antibiotic therapy was changed into Linezolid, Cefepime and Ciprofloxacin. During the first month in our ICU, two episodes of hemorragic shock occurred and were solved thanks to traditional therapy. Furthermore, atrial fibrillation with rapid ventricular response was treated with electrical cardioversion a few times. Four days later fever persisted and sepsis markers were high: septic shock was diagnosed. Renal replacement therapy (CVVHDF) was performed days later because of acute renal failure. Additionally, laboratory investigations revealed an impaired liver function accompanied by hyperbilirubinemia (15 mg/dl) and increased hepatic markers. Serological tests for hepatitis virus showed the patient was infected with the HAV, so Caspofungin was added to the ongoing drug therapy. Subsequentially, the decision was made to use the CytoSorb hemoadsorption cartridge in hemoperfusion mode with Plasmapher Apherlungs machine (Figure 1).

Results: The therapy lasted 24 hours and, after that, bilirubin and LDH values decreased from 16.11 to 12 mg/dl and from 502 to 400 UI/L, respectively. Days later bilirubin levels dropped progressively (6.38 mg/dl) and LDH levels stabilized, until both of them reached their physiological ranges. The patient's general condition improved impressively and weaning from mechanical ventilation and inotropic drug therapy was made. After 104 days in our ICU, the patient was finally discharged.

Conclusions: In this case describing the use of CytoSorb in hemoperfusion mode in a patient suffering from an overshooting

Fig. 1. CytoSorb cartridge at the end of the treatment (for Abstract no P32).

inflammatory response and liver dysfunction, treatment was associated with improvement in hemodynamic, inflammatory status as well as liver function. The setup was technically feasible and the treatment was performed without any complication. Further studies are needed in order to investigate on bilirubin and cytokine removal in such critical patients.

Rhabdomyolysis

P33

Use of Haemoadsorption with Cytosorb in Patients with Severe Acute Rhabdomyolysis: A Case Series

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Background: Rhabdomyolysis (RML) is an interdisciplinary condition due to muscle cell injury followed by the release of cell components into circulation (myoglobin, CPK, etc). Etiology of RML has a broad range; a serious complication is acute kidney injury (AKI). In the acute phase treatment should be aimed at preserving renal function and restoring metabolic derangement. Use of haemoadsorbtion with Cytosorb should be considered when hypermyoglobin could seriously compromise patient life.

Aim of this paper is evaluate capability to remove myoglobin and trend of adsorption of this technique in patients with RML.

Methods: We evaluate 13 treatment with Cytosorb in 8 patients with RML (due to crush syndrome, myopathy or infective myonecrosis) enrolled in this observational trial.

We performed a baseline systemic blood test to measure systemic myoglobyn and a pre- and post filter. Data were incorporated by 3 hours steps from the beginning of Cytosorb filter treatment. Duration of treatments was variable from 10 hours to 27 hours.

We analyzed total removed myoglobin as the cumulative amount of myoglobin extracted by the system, myoglobin extraction rate and the percentual ratio of the difference of pre- and post-filter myoglobin concentration. We used SPSS v.25 for statistical analysis. One way Anova was chosen for the analysis between time steps.

Results: During the 13 treatment performed, average amount of myoglobin removed was 784,925 mcg (DS 704,740; range 31,925–2,129,614). Removal rate does not show a significant statistical decrease in the 27 hours of treatment ($p = 0.414$); amount removal in the unit time and the removal rate was directly proportional to the blood concentration of myoglobin. Total amount of removal myoglobin is represented in the graphic n.1 (Fig. 1).

Discussion and Conclusions: This technique has proved to be able to remove myoglobin in patient with RML. Removal rate during each single treatment results rather variable and it could depend on many factors that impact on the binding of myoglobin and resin of the filter (es. pH, competition of molecules). A higher plasmatic concentration of myoglobin however results in an increased mass clearance. In view of the negative trend of removal rate, probably a broader casuistry may show a decrease in the system performance. Range of cases are still limited and that explains the large standard deviation of each point; however final results show the benefit of this technique. At this time, amount of systemic myoglobin at which begin haemoadsorption treatment cannot be defined. Probably this will be subject of future studies.

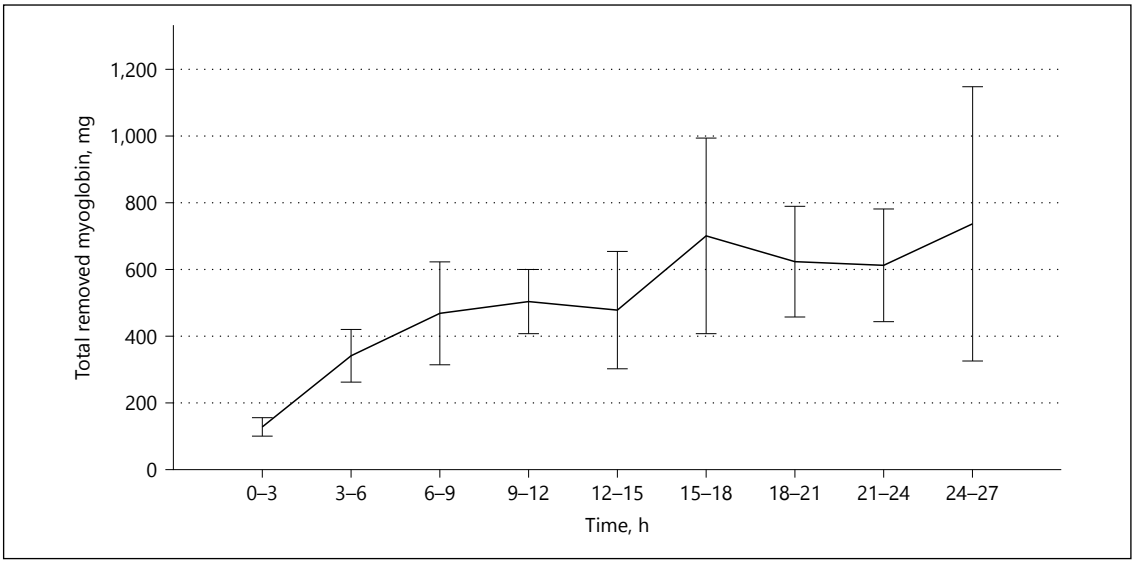

Fig. 1. Total amount of removal myoglobin (for Abstract no P33).

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P34

Critical Illness Myopathy after septic shock in *Pneumococcal* pneumonia: Rhabdomyolysis Treatment with Cytosorb Cartridge

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Background: Critical Illness Myopathy (CIM) is a major complication in critically ill patients due to muscle weakness, energetic dysfunctions and many other factors [1]. Pro-inflammatory cytokines and metabolic imbalance as well as malnutrition and drugs are the trigger of these processes [2]. The severity of muscle weakness is widely variable and might be associated with symptoms of paralysis. Monitoring necrosis muscular enzymes levels (i.e. LDH, AST, ALT, Myoglobin, CK) is critical in order to understand the evolution of the myopathy. Blood purification adjuvant techniques might be useful to control their levels, eventually protecting at the same time renal function.

Case Presentation: We present the case of a female patient, 68 years old, with a complex picture compatible with a suspected CIM resulting from a previous solved episode of septic shock in Pneumococcal pneumonia. Anamnesis underlined arterial hypertension, chronic obstructive pulmonary disease (COPD), hypercholesterolemia, obesity and cannabis use. Prior the admission in our Intensive Care Unit, the patient was treated in a peripheric hospital for a septic shock condition, presenting severe respiratory failure, cardiocirculatory dysfunction, oliguria and severe lactic and metabolic acidosis. Then the patient was transferred in our department, presenting an instable condition with right hemopneumothorax, severe hypoxemia (PaO2/FiO2 150 mm Hg) and requiring noradrenaline administration (0.5 μg/kg/min). SAPS II score was 58, corresponding to a predicted mortality of 64%.

In the next days, after thoracic drainage and bronchoscopy, hemodynamic stabilization was obtained and sedation suspended. The patient was awake and alert but developed severe tetraplegia with only elbow flexion and extension of the toes. At the same time, an increase in necrosis muscular enzymes and transaminases was observed. Needle electromyography (EMG) testing highlighted a suspected myopathy without sign of denervation and muscle biopsy was prescript to understand the myopathy etiology once the patient recovered from the rhabdomyolysis.

On Day 12, in front of the persistent increase in muscle enzymes and limited renal function (diuresis <200 ml/day), blood purification with Cytosorb adsorber was started in combination of a CRRT treatment for myoglobin and CK removal. The treatment was performed for three consecutive cycles for total of 72 hours.

Results: The course of standard laboratory muscle markers and myoglobin levels are shown in Table 1. At the end of the three Cytosorb treatment, we observed an important decrease in circulating myoglobin and CK levels, respectively 78% and 87%. More-

Table 1. Muscle enzymes and transaminase course (Day from admission in ICU) (for Abstract no P34)

	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19
Myoglobin (μg/L)	16,082	14,996	13,258	14,363	–	13,955	19,373	11,404	8,716	4,904	4,334	1,061	1,061	689	350
CK (U/L)	6,551	7,009	5,852	4,679	4,962	5,100	5,900	3,021	3,589	2,272	736	439	439	299	220
LDH (U/L)	409	424	394	477	599	–	628	655	880	968	919	919	866	–	–
AST/GOT (U/L)	322	365	335	336	390	–	382	320	382	305	184	184	141	125	99
ALT/GPT (U/L)	219	266	290	358	424	–	405	357	455	437	354	354	305	271	230

over, muscle enzymes continued to progressively improve over the following days, until reaching normal levels. On Day 13, renal function restored with diuresis recovery (1500 ml/h), avoiding any further kidney impairment. A slow progressive increase in limb mobility was observed.

Conclusion: Cytosorb represents an easy support in case of rhabdomyolysis for a rapid removal of myoglobin and CK from blood and other muscle parameters stabilization, preventing at the same time further renal damages due to myoglobin nephrotoxicity.

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P35

Treatment of Post-Traumatic Rhabdomyolysis with a Combined Purification Strategy: A Case Report

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Background: Crush syndrome or traumatic rhabdomyolysis, a medical condition characterized by major shock and renal failure after a crushing injury to skeletal muscle is a challenge for intensivist.

Methods: We present a case regarding a young man (19 years old) victim of a motorbike accident in urban environment. He was conducted by emergency equipe (i.e. 911) in local emergency department. At admission he was awake and collaborative, with retrosternal/epigastric pain, and exposed fracture of the left knee with important lesion of the popliteal artery, low arterial pressure. Total body TC was performed: rupture of the diaphragm with herniation of the stomach, lung contusion, hemoperitoneum, right acetabulum and whole iliac wing fracture, confirmed left knee fracture with vascular lesion (ISS66).

Urgent surgery was immediatly performed under general anaesthesia: reparation of the diaphragmatic rupture with stomach repositioning, correction of intraperitoneal hemorrage (from mesenteric artery), urgent vascular graft of the poplitea artery. The patient was conducted in ICU.

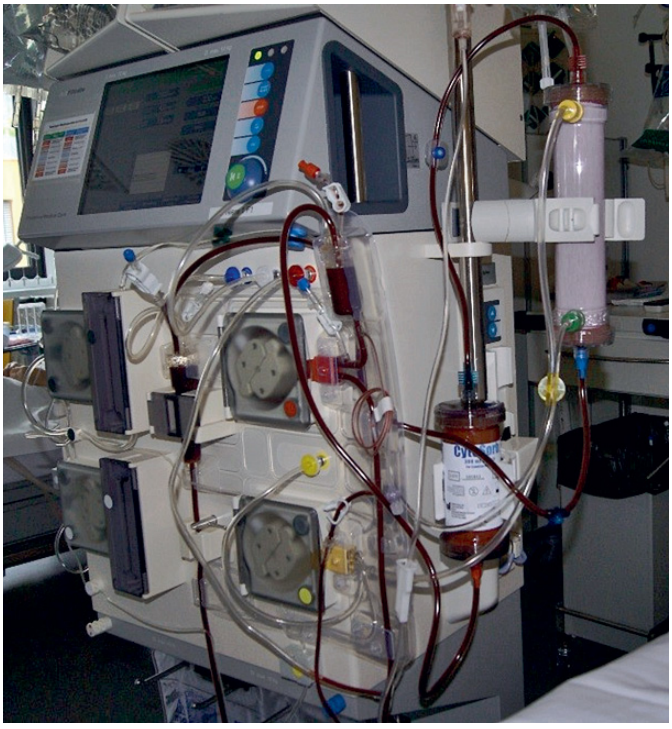

Fig. 1. CVVHD plus Cytosorb (for Abstract no P35).

He was sedated and curarized, under mechanical ventilation. Routine emergency Laboratory test was performed, and we notice low Hb level and an increasing value of myoglobin (up to 60000 mg%), with a rapid and progressive worsening of renal function, suggestive for AKI. So we started Continuous Renal Replacement Therapy in CVVHD CiCa using an highly adsorbent cartridge in order to remove Citokines and myoglobin (Citosorb®) and a secondary high-cut off dyalisis filter (Emic2®). Two filters were mounted in series. We used an HFCVC in IJV dx only for CRRT; a CVC was inserted in IJV sx and subsequently a PICC in antecubital vein, in order to avoid turbolent blood flow in superior vena cava.

Results: A fall in myoglobin plasmatic dosage (24000 mg%) was observed after two days application of this strategy; the patient recovered his renal function up to spontaneous diuresis. We did not observe any complication in hemodynamic status, hepatic function, pH balance and coagulation cascade.

Conclusions: Although there are no randomized studies, we can conclude that in crush syndrome the early use of specific adsorbent resins associated with high cut-off dialysis filters has played a decisive role in breaking down myoglobin levels and in the recovery of renal function, drastically reducing the potential damage caused by rhabdomyolysis.

Surely it will take time for large-scale studies to determine what is the optimal treatment, even in terms of timing, of the crush syndrome, however we can suggest the early use of this strategy in cases like the one just discussed.

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Pediatric Patients

P36

First Hemoadsorption Using CytoSorb in a Pediatric Patient with Toxic Epidermal Necrolysis

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Background/Aims: Toxic epidermal necrolysis (TEN) is an adverse drug reaction associated with the separation of skin and mucous membranes at the dermal-epidermal junction. TEN is characterized by widespread keratinocyte apoptosis and necrosis: the major histocompatibility compless class I leads to clonal expansion of CD8+, which infiltrate the skin while soluble factors (TNF-, INF-γ and iNOS) induce apoptosis. The disease is extremely rare but particularly serious: mortality is 20 to 25% during acute phase, and from 30–35% at one year. Treatment is essentially supportive, as no effective etiological treatment has been identified.

Methods: We describe a case of a child 8 years-old with an extremely severe clinical picture of TEN (>95% of BSA), SCORTEN score 5 (estimated risk of death ≥90%).

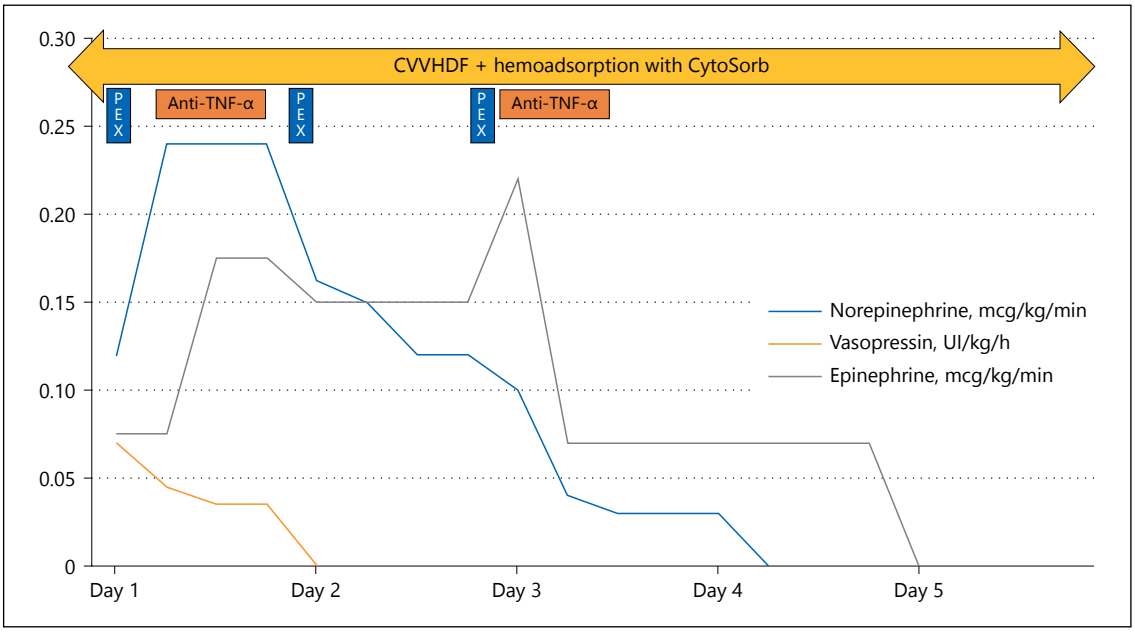

Fig. 1. Vasopressors and inotrope trend during extracorporeal blood purification (for Abstract no P36).

Results: The child was admitted in emergency department for purpuric macules in the upper trunk and in the face with a rapid spread to a confluent erythema. The family reported oral intake of cephalosporins a week ago. After 24 hours the child developed a progressive respiratory distress and he was transferred in PICU with need of tracheal intubation. The dermatological picture evolved to a extensive detachment of sheets of epidermidis associated to an erosive and hemorrhagic mucositis and he became deeply hypotensive with need of high doses of catecolamines (Adrenaline 0.15 mcg/kg/min, Noradrenaline 0.25 mcg/kg/min, Vasopressin 0.07/UI/kg/h) associated to iperlactatemia (4.5 mmol/l) and metabolic acidosis. Then for massive pulmonary edema and refractory hypoxia a VA ECMO was started. For the rapid evolution of the clinical picture despite the supportive care we decide to start an hemoperfusion with CytoSorb associated to CVVHDF to manage fluid overload. Hemoperfusion continued for 120 hours with three session of plasma-exchange and two administrations of anti-TNFα (1st and 4th days). During these 5 days we assisted to a significative reduction of vasopressors and inotropes (Figure 1). At 18th day he was weaned from ECMO support: unfortunately he died a week later due a Acinetobacter Baumanii septic shock.

Conclusion: Considering that the pathophysiological process of TEN is by drug-induced cytotoxic T lymphocytes, hemoperfusion can remove soluble-mediators without the potential risks of the transfusion-associated therapies of plasma-exchange. Previously positive experiences of intermittent hemoperfusion in TEN has been already described. We describe the first use of CytoSorb in a pediatric patient with TEN: CytoSorb offered the opportunity to perform a continue hemoperfusion along 24 hours showing beneficial effect on hemodynamic stabilization. Our clinical case was characterized by an extremely severe clinical picture of TEN requiring also an ECMO support, although he died for an infectious complication correlated with the high surface of denuded skin, the patient overcame the acute phase with the combination of supportive and immunomodulatory treatment, based primarily on the hemoperfusion with CytoSorb.

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P37

Rapid Treatment of Unexpected Septic Shock: A Single Pediatric Case Recovery for Septic Shock Due to Streptococcal Arthritis Using Early Extracorporeal Cytokine Adsorber Treatment

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Background and Aims: We present a case of a male patient, aged 11 months, hospitalized in our Pediatric Hospital Giovanni XXIII (Bari) and evaluated at admission for a huge right knee edema, caused by β-Hemolytic Streptococcus and Staphylococcus Aureus and developed in septic shock within 12 hours after the admission. The patient was transferred in Pediatric ICU in pre-agonal conditions, refractory to septic shock conventional treatments. After parental consent, we added, as life saving treatment, the extracorporeal cytokine absorber (Cytosorb). After 2 sets of 18 hours, we obtained a massive reduction of inflammatory mediators and cathecolaminic support, an improvement of PRISM III, SOFA Score, respiratory and metabolic parameters. After 5 days the patient was transferred.

Material: Twelve hours after the admission the patient presented hypotension, tachycardia, dyspnea and tachypnea, fever, anuria, cyanosis of the extremities, diffused petechiae and low neurological response to stimulation (Table 1). Blood gas analysis showed pH 7.19, $PaCO_2$ 55 mm Hg, PaO_2 75 mm Hg, lactate 5.5 mmol/L, Be –12 mmml/l. On arrival in ICU peripheral, central and radial catheters were inserted. After sedation and curarization the patient was intubated and ventilated in PC – Mode. Laboratory exams defined high values of Proteine C Reactive; Lactate, hyperfibrinogenemia and thrombocytopenia. Pulmonary thickening was at the chest radiograph. The clinical condition was refractory to high inotropic, vasopressor and diuretic support; to crystalloids, blood, plasma, albumin infusion. Temperature 39°C and broad spectrum antibiotic therapy not even related to blood cultures started. Mechanical cooling and maximal ventilatory support had no result. A continuous renal replacement therapy (CRRT) using a nephrological device (Prismaflex System, Germany) was started and, after parental consent, an emoadsorbent cartridge (Cytosorb) was integrated in post-hemofilter position in the traditional circuit. Continuous veno-venous hemodiafiltration (CVVHDF) flow ranged from 20–30 ml/kg/h, ultrafiltration rate was variable with hemodynamics; heparin anticoagulation (5–30 IU/Kg/h) was controlled with activated clotting time (ACT: 150–200 sec), APTT-INR (1.5–1.8), Thromboelastogram, every 4 hours. Every treatments had a duration of 18 hours with 24 hours of interval, to verify improvements in PRISM III and SOFA score. Clinical and biochemical parameters were measured daily. CVVHDF was continued for 3 days. After 4 days of respiratory weaning, without cardiac drug support, the patient was extubated and in 5 days was transferred to the pediatric ward.

Results: The dosage of Norepinephrine was reducted after the second treatment and stopped after 24 hours. Contextually there was the reduction of inflammatory mediators, PRISM III and

Table 1. Patient's data before, during and after the treatments (for Abstract no P37)

Patient Data at Admission		Patient Data before, during and after treatment			
Hypotension	MAP <40 mm Hg	Data	Before 1st Treatment	After 1st Treatment	After 24 hours
Tachycardia	175 bpm				
Fever	38.8°C	*Norepinephrine*	0.05 μg/kg/min	0.03 μg/kg/min	0
GCS	7	*IL-6*	140 pg/ml	0.5 pg/ml	0.5 pg/ml
pH	7.19	*TNFα*	351 pg/ml	38 pg/ml	0.5 pg/ml
PaCO2	55 mm Hg	*SOFA Score*	27	10	
PaO2	75 mm Hg	*PRISM III Score*	18	9	
Lactate	5.5 mmol/L				
BE	–12 mmol/L				
PRC	480 mg/dL				
PLT	50,000				

SOFA Score with an improvement of metabolic, respiratory and hemodynamic status (Table 1).

Conclusions: The immediate use of CytoSorb allowed to obtain a rapid improvement of the hemodynamic conditions, renal and pulmonary function, reduction of vasopressors and resolutive reduction of "cytokines storm", a not rare deadly event even in pediatric patients.

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P38

Extracorporeal Blood Purification with Cytosorb® in Pediatric Refractory Septic Shock: Does It Make the Difference?

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Background: Severe sepsis and septic shock is the most common cause of pediatric death in the world. The combination of different extracorporeal blood purification (EBP) techniques has been suggested as a potentially effective approach in the management of septic shock.

Methods: We present a case of a 8-year-old patient affected by acute lymphatic leukemia and treated with recent chemotherapy, admitted to our Pediatric Intensive Care Unit (PICU) for severe refractory septic shock correlated to Clostridium difficile infection.

Results: While in Hematology ward, the patient developed severe neutropenia and fever. Empiric broad spectrum antimicrobial and antifungal therapy – with vancomycin, meropenem, metronidazole and micafungin – was started. A progressive deterioration of general conditions occured, rapidly leading to severe septic shock. Then, the patient was transferred to our PICU for intensive treatment.

At admission, he presented extreme and persistent hypotension, with mean arterial pressure (MAP) below 40 mm Hg, and severe metabolic acidosis with hyperlactacidemia (arterial lactate levels of 160 mg/dl). He underwent orotracheal intubation, mechanical ventilation and cardiocirculatory support.

Despite important fluid resuscitation (>20 ml/kg), inotropic therapy (epinephrine 0.2 μg/kg/min) and hydrocortisone administration (1 mg/kg x 4), the clinical condition did not improve.

Even in absence of acute kidney injury, continuous renal replacement therapy (CRRT) was started, in order to counteract the severe metabolic acidosis and fluid overload, due to capillary leakage, and to remove sepsis cytokines. Continuous veno-venous hemodiafiltration (CVVHDF) modality, with a high effluent dose of 60 ml/kg/h, combining a ST60 filter with Cytosorb® cartridge column, was chosen.

After 48 hours from the beginning of this EBP strategy, a significant reduction in inotropic drug doses (epinephrine from 0.2 to 0.04 μg/kg/min), lactates (from 160 to 12 mg/dl), PCR (from 22 to 3.5 mg/dl) and procalcitonin (from 8 to 1.5 ng/ml) levels was observed.

CRRT was continued for the first 72 hours without complications. Finally, the patient was successfully discharged from PICU after 9 days.

Conclusions: Cytosorb® is a cartridge column with a wide surface area which can directly adsorb and clear sepsis mediators. The combination of CRRT and Cytosorb® has a relevant synergistic effect also in pediatric septic shock, helping in the management of cardiocirculatory shock, metabolic acidosis, fluid overload and immuno-modulation.

Uremic Toxins

P39

Indossyl Sulphate and P-Cresol Sulphate Effective Removal by Divinylbenzene Resin in Patients in Hemodialysis

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Background/Aims: High serum levels of indoxyl sulfate (IS) and p-cresol sulfate (PCS), nephrovascular uremic toxins, are associated with high risk of cardiovascular disease in hemodialysis (HD) patients. IS and PCS circulate in the blood stream mainly bound to albumin (>90%) and minimally as free solutes and accumulate in patients with chronic and terminal renal disease. The high affinity of IS and PCS for albumin makes their removal from the blood very critical through conventional dialytic techniques.

The aim of this study was to evaluate the efficacy of a symbiotic integrator and divinylbenzene resin in the reduction of serum IS and PCS levels.

Methods: *In vitro:* an experimental solution (3.5 L, pH 7.4) containing bovine serum albumin, IS and PCS with analogous concentrations to those of hemodialysis patients, was circulated (flow of 300 mL/min) in a closed circuit including the resin to be tested (DVB coated with polyvinylpyrrolidone and Cellulose functionalized with hexadecyl chains) for 5 h. Total and free IS and PCS concentrations were quantified by tandem mass spectrometry (LC/ESI-MS/MS) every hour until the end. IS and PCS removed amount was evaluated by applying the mass balance formula and the total percentage reduction formula. The albumin concentration was evaluated by the Bradford method.

Trial: randomized placebo-controlled single blind pilot trial in HD patients. 13 patients in traditional HD were randomized to take the symbiotic NATUREN G (n = 7) or placebo (n = 6) for 2 months, and subsequently undergoing dialysis with PS-DVB resin. After enrollment of the symbiotic (T2) and after dialysis with PS-DVB (T3), routine blood count parameters and serum IS and PCS levels were evaluated at enrollment (T0).

Results: *In vitro:* In vitro, DVB resin is more effective in removing total IS and PCS (56%, 51%) and free (70%, 77%).

Trial: 11 patients completed the study. Early treatment with the symbiotic does not vary serum IS and PCS levels. Dialysis with DVB resin reduces serum IS and PCS levels (38% vs 27%, p = 0.04, 31% vs 23%, p = 0.02, Figure 1) compared to traditional dialysis.

Conclusions: Dialysis with DVB reduces serum IS and PCS levels to a greater extent than traditional dialysis. To confirm the results obtained, long-term experimentation is expected in a larger series of patients.

IBD

P40

Efficacy and Safety of Leukocytapheresis Adsorber Device LA25: Experience with 9 Patients

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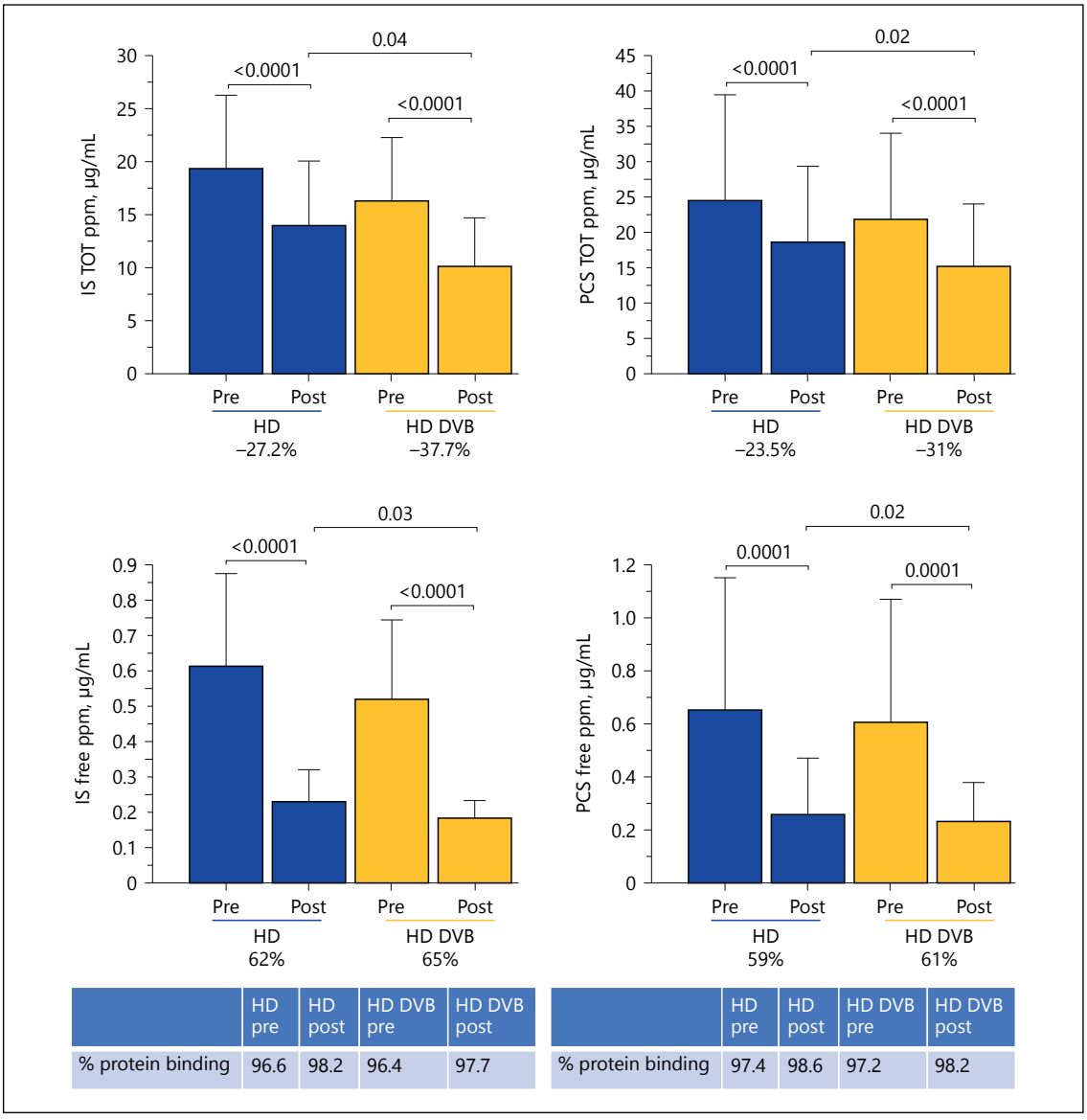
Background/Aims: Inflammatory Bowel Diseases (IBD), i.e. Crohn's disease (CD) and Ulcerative Colitis (UC), are chronic inflammatory disorders, impairing both digestive function and patient quality of life. The etiology is still not completely understood, but induction and perpetuation of IBD inflammation with activation of inflammatory markers is crucial. Increased leukocytes levels are typical, since, once migrated from the peripheral blood to the intestinal wall, they participate into the inflammatory cascade and cause bowel damage. Therapeutic strategies are essentially based on immunosuppressive and anti-inflammatory drugs. In recent years, selective depletion of myeloid lineage leucocytes by adsorptive leukocytapheresis have been applied as a non-pharmacologic treatment strategy. LA25 aphaeresis (Leukocyte Adsorber 25), distributed by Aferetica, is an effective and safe method for IBD patients who showed inadequate response or intolerance to conventional therapy.

Methods: Between May 2016 and December 2018, 9 patients (3 female and 6 male, 2 CD and 7 UC, average age 56.6 years) have been treated with LA25 leukocytapheresis. 3 other patients were excluded due to absolute contraindication (severe cardiac disease). The indication for leukocytapheresis were: active disease (4), refractory disease (3) and oncological comorbidities (2). Overall, 8 patients had some contraindication to conventional IBD therapies.

All patients received 5 weekly apheresis session using LA25, each one at 30 mL/min flow rate for 60 min, with a final volume of 1.8 L of peripheral venous blood processed per session. 5 patients received 1 monthly maintenance apheresis for an average of 8 months. Concurrent therapies included mesalamine (9) and steroids (7), while 2 patients were in thiopurines.

We evaluated patients at the beginning of therapy, then after 3 and 12 months.

Results: After apheresis treatment, clinical disease activity indexes, both for CD (Harvey-Bradshaw Index – HBI) and UC (Mayo partial score – MPS) decreased from moderate to mild (HBI from 10 to 6, MPS from 6 to 3). Blood parameters levels changed as follows after 3 months: white blood cells 6.82/7.38, haemoglobin 144/123, MCV 93.8/94.4, platelets 223/263, VES 19/17, PCR 0.6/0.6, faecal calprotectin 481/269. After 3 month, 7 patients achieved an improvement of endoscopic activity, 4 (out of 7) patients withdrew steroids, and 3 (1 CD, 2 UC) patients achieved clinical remission. Between patients who received leukocytapher-



	HD pre	HD post	HD DVB pre	HD DVB post
% protein binding	96.6	98.2	96.4	97.7

	HD pre	HD post	HD DVB pre	HD DVB post
% protein binding	97.4	98.6	97.2	98.2

Fig. 1. Results of the in vivo trial (for Abstract no P39).

esis as maintenance therapy, we observed in 4 a relapse of disease at a median of 4 months while 1 UC patient showed a persistent disease remission after 16 months (ongoing). There were no adverse side effects documented with these extracorporeal circulation procedures.

Conclusion: Leukocytapheresis using LA25 is safe and easy to perform and permits a clinical and endoscopic response in the majority of IBD patients. Due to its safety profile, it can be indicated in patients with high risk of complications using standard therapy or biologics.

P41

Combination Therapy with Leukocytoapheresys and Vedolizumab in a Patient with Ulcerative Colitis Refractory to Anti-TNFs

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Background and Aims: Leukocytes (neutrophils, monocytes/macrophages) are major actors in the pathogenesis of IBD, since, once migrated from the peripheral blood to the intestinal wall, actively participate into the inflammatory cascade by releasing cyto-

kines ultimate responsible for bowel damage. The recruitment of leukocytes is increasingly becoming a target for IBD therapy from leukocytoapheresys to anti-integrins and SP1-inhibitors. Moreover, the idea of combining multiple therapies with different mechanisms of action to get a deeper control of inflammation and potentially modify the course of IBD is receiving growing attention by medical researchers. We report a patient with steroid-dependent UC, failure to anti-TNFs, successfully treated with leukocytoapheresys and vedolizumab.

Methods: We report a case of a 45-year-old woman with a diagnosis of ulcerative proctitis. Due to the onset of steroid dependency, clinical and endoscopic worsening, she was put on infliximab induction and maintenance, optimized every 4 weeks because of loss of response; switched to adalimumab without benefit (primary nonresponse). In October 2016, we decided to swap to vedolizumab. Azathioprine 2.5 mg/kg. was added in December 2016, but disease remained active. She refused colectomy. In February 2017, we decided to submit the patient to therapeutic GMA as adjuvant therapy. The patient received 5 weekly apheresis sessions using LA-25 (Leukocyte Adsorber 25), each ones at 30 ml/min flow rate for 60 min, with a final volume of 1.8 L of peripheral venous blood processed per session. A significant improvement of symptoms was reported after the fourth session. Partial Mayo score was 9 at the first session, and 5 after the fourth.

Results: The patient achieved steroid free remission and mucosal healing (Mayo subscore 1 after 1 year). Azathioprine has been stopped and she is still on vedolizumab monotherapy. No adverse events occurred.

Conclusion: We suggest an adjuvant role of GMA in combination therapy with vedolizumab (a drugs which shows a slow onset of action in real life). A previous published case had been treated with an intensive apheresis protocol, unsustainable in terms of costs. In our patient, a standard apheresis protocol was adopted as suggested by both the manufacturer and previous literature, with equal effectiveness. Apheresis can speed up the response to vedolizumab by selective depletion of activated leukocytes, further reducing cell trafficking. Being a non-pharmacological approach, with no relevant safety signal, the adjunct of apheresis to biologics could represent a valid option in patients with UC difficult to treat, with inadequate response to biologics, and should reduce the need of colectomy. This hybrid approach has been used in small case series in combination with anti-TNF, especially adalimumab, and recently in Crohn's disease with ustekinumab, but, in our opinion has a more appealing rationale in combination with anti-integrins due to a synergistic mechanism.

P42

Combination Therapy with Leukocytoapheresys and Vedolizumab in Patients with Ulcerative Colitis Refractory to Anti-TNFs

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Background and Aims: The recruitment of leukocytes has become a target for IBD therapy from leukocytoapheresys to anti-integrins and SP1-inhibitors. Combining multiple therapies with different mechanisms of action to get a deeper control of inflammation is receiving growing attention by medical researchers, but safety concerns are an issue. Being a non-pharmacological approach, with no relevant safety signal, the adjunct of apheresis (GMA) to biologics could represent a valid option in patients with UC with inadequate response to biologics, and should reduce the need of colectomy. This hybrid approach has been used in small case series in combination with anti-TNF, especially adalimumab, and recently in Crohn's disease with ustekinumab. Two case reports (one from our group) have been published reporting combo therapy with the antiintegrin vedolizumab. This association has a more appealing rationale due to the synergistic mechanism and on the basis of the slow onset of action of vedolizumab observed in everyday practice. Apheresis can speed up the response to vedolizumab by selective depletion of activated leukocytes, further reducing cell trafficking.

The aim of this study will be the assessment of efficacy and safety of combo therapy with leucocytoapheresys and vedolizumab in patients with UC refractory to conventional therapy and anti-TNFs.

Methods: Study population: patients 18–75 years with steroid-dependent/resistant UC refractory to conventional therapy and failure or intolerant to anti-TNFs, who have completed vedolizumab induction therapy (week 8), with inadequate response (Mayo score >4).

Investigational product: therapeutic GMA (5 weekly apheresis sessions) using LA-25 (Leukocyte Adsorber 25, Leuc@pher).

Type of study: open label, multicenter.

Recruitment period: one year.

Assessment of disease activity (at induction, at week 8, at the end of GMA, at 52 weeks): Mayo score full and endoscopic subscore.

The IBDQ score will be also assessed at the beginning and after GMA sessions.

Primary objectives: to achieve steroid-free remission at week 16 and 52.

Secondary objective: to evaluate safety of GMA plus vedolizumab; to evaluate the impact on quality of life.

Results and Conclusion: We aim to demonstrate an adjuvant role of GMA in combination therapy with vedolizumab in moderate-to-severe UC who have failed conventional therapies and are refractory or intolerant to anti-TNFs. The ultimate goal will be the avoidance of colectomy, which still has disabling sequelae and a significant impact on quality of life.

Immunological pathologies

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Cascade Filtration, a Promising Treatment for Myasthenia Gravis

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Background/Aims: Myasthenia Gravis (MG) is an autoimmune disorder characterized by muscle weakness. Circulating antibodies against the nicotinic acetylcholine receptors (AChR) of the neuromuscular junction are present in most patients and their pathogenicity was clearly demonstrated. A little percentage of patients were defined seronegative that studies suggest be means as unrecognized antibodies. Thymectomy in conjunction with immunosuppressants is used as the first choice of therapy. Nevertheless, in those patients who do not respond to this treatment and who require assisted ventilation, plasmapheresis represents a successful technique.

Cascade Filtration can non-selectively remove immunoglobulins containing antibodies, with the aim of reducing its concentration and consequently improving muscle strength and subjective symptoms.

Methods: Cascade Filtration was carried out using the automatic system Plasmapher/Apherlungs (Aferetica, Italia), directly connected with Amicus Separator System (Fresenius Kabi, Italia). Plasma obtained by centrifugation is conveyed into a fractionator filter, Evaflux 3A20 (Aferetica, Italia), which allows a semi-selective plasma purification and removes immunoglobulins containing AChR antibodies. After purification, plasma goes back to the patient. We treated 2 patients seronegative with severe MG, showing albumin allergic reactions. During the plasma purification procedures, the blood flow was kept at 50 ml/min and the flux rate of the filtration in the plasma separator was 20 ml/min. Plasma fractionation was performed with about 1 plasma volume at each session. Treatments were performed every six weeks for the firts patient and every four weeks for the second patient, as a maintenance therapy.

Results: after plasmapheresis treatment, remarkable clinical improvements were observed.

Apparent and rapid recovery from myasthenic muscle weakness was observed and subjective symptoms, especially chest compression and general fatigue, were significantly more attenuated with Cascade Filtration treatments.

Unfortunately, it has not been possible to calculate the decrease in the AChR antibodies titer and to collect objective data. Therefore, our short experience shows a prolonged time of apheresis as maintenance therapy.

Conclusion: in the present case series we could demonstrate that Cascade Filtration, performed with fractionator filters Evaflux 3A20, can really improve subjective symptoms of patients with Myasthenia Gravis. Cascade Filtration is an effective and safe treatment for patients with severe generalized Myasthenia Gravis, who show inadequate response to pharmacological therapy and therapeutic plasma-exchange or present allergic reactions to albumin administration, also thanks to the fact that Cascade Filtration, avoiding plasma substitution, reduces transfusion-related risks.

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Utility of Double Filtration Plasmapheresis in Acute Antibody Mediated Renal Allograft Rejection

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Background: Double filtration plasmapheresis (DFPP) is a special form of membrane filtration, used in the setting of ABO blood group incompatible kidney transplantation and in patients with antibody-mediated acute renal allograft rejection (AAMR).

Methods: We describe the use of DFPP as a component of anti-rejection treatment regimen. The evolution of patient renal function was evaluated during the hospital admission.

Moreover, we developed an *in vitro* study using anti-HLA/DSA antibody on endothelial glomerular cells (HGECs) to evaluate protective effect of DFPP in microvascular injury induced by antibody-link and Complement-cascade activation. Sera of patient were stored at 0 time and before and after every DFPP session. The inflammatory state was evaluated analyzing Complement activity (C5b9), the expression of adhesion molecules VCAM-1, E-selectine and CD40 (FACS analysis) and the adhesion of PBMCs and NK cells on Matrigel-coated plates. The effect of DFPP on apoptosis were analyzed using TUNEL assay (% of apoptotic cells).

Moreover, were evaluated the pro-angiogenetic effects on HGECs analizing the N° of capillary-like structures for field.

Results: A 42-year-old male who had been on hemodialysis by 1991 due to nephronoptisis and with a previously renal transplant lasted from 1995 to 2004, underwent to a IInd deceased-donor kidney transplantation. He was HCV positive without severe hepatic injury. After transplantation, he had detrimental renal function without presence of DSA and with vPRA 86.2% cl I. His maintenance immunosuppressive regimen included tacrolimus, prednisone and MMF. Percutanous allograft biopsy revealed AAMR. Two cicles of intravenous immunoglobulin (IVIG) along with alternate day DFPP (five sessions) and two cicles of antiCD20 (Rituximab) 1 g were applied. The patient was disharged with stabilized graft function (sCR about 3.2 mg/dl).

The *in vitro* study demonstrated the reduction of inflammatory state and of Complement-cascade activation after DFPP treatment (reduction of % of positive cells for MAC, lower expression of VCAM-1, E-selectine and CD40 and reduced N° of adherent PBMCs and NK cells after DFPP treatment), the reduction of apoptosis and the pro-angiogenetic effects of DFPP treatment.

Conclusions: DFPP inhibit microvascular injury induced from antibody-link on endothelial cells and by activation of Complement-cascade, through antibodies against donor removal and inhibiting Complement activation and related apoptosis activation, NK cells adhesion and promoving angiogenesis preserving renal function.

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