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Abstract Book of the

4th Workshop Purification Therapies

From Research to Clinics "The End of the Beginning"

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Executive Summary

Over recent decades, advances in medicine have transformed the management of systemic diseases, severe inflammatory syndromes, and end-stage organ failure, expanding therapeutic possibilities in intensive care and transplantation. The fourth Workshop on Purification Therapies (WPT25), entitled "From Research to Clinic: The End of the Beginning", marked an important moment in the maturation of extracorporeal blood purification therapies (EBPTs) and organ perfusion technologies. The first day focused on dysregulated inflammatory diseases and EBPTs, highlighting the role of inflammatory mediators as cytokines, pointed out the potentiality in their clinical applications in septic and cardiogenic shock. The discussion was focused on patient selection, timing, dosing, and drug–device interactions. The second day addressed organ preservation and regeneration, emphasizing *in situ* and *ex situ* perfusion strategies to expand donor eligibility—including DCD and extended criteria donors—while mitigating the iatrogenic effects as the ischemia–reperfusion injury. Discussions explored temperature management, inflammatory modulation during procurement and treatment, and future perspectives such as personalized perfusion protocols and xenotransplantation. With 550 participants, 26 oral presentations, practical workshops, and 161 scientific contributions published in one special issue of Transplant International, the meeting consolidated evidence and try to define priorities for integrating purification and perfusion therapies into clinical practice. Abstracts from the meeting are published in Transplant International: "Abstract Book of the 4th Workshop Purification Therapies From Research to Clinics "The End of the Beginning", September 19th-20th, 2025." at https://www.frontierspartnerships.org/research-topics/197/aferetica—wpt-2025-meeting-abstract.

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4th workshop purification therapies, from research to clinics "the end of the beginning": executive summary

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Keywords
Blood purification, cytokines adsorption, *ex-situ* perfusion, organ regeneration, perfusion machines

Medicine has made extraordinary progress over the past decades, enabling the management and eradication of diseases that once represented a major burden for previous generations. These advances now allow us to treat systemic diseases and syndromes that until recently would have been considered terminal. This includes severe organ failure resulting from dysregulated inflammatory responses in critically ill patients, as well as organ failure that can only be resolved through transplantation.

Substantial progress has been achieved in both scientific knowledge and technological development in these fields, opening new clinical possibilities. Nevertheless, significant challenges remain in Transplant Medicine and Intensive Care, stimulating the development and progressive implementation of novel therapeutic strategies.

In this context, the fourth edition of the Workshop on Purification Therapies (WPT25) – *From Research to Clinic: "The End of the Beginning"* – aimed to

contribute to scientific and clinical advancement in the development, validation, and implementation of new therapies in organ transplantation and dysregulated inflammatory diseases. The history of these meetings, initiated more than a decade ago, has progressively evolved from the discussion of exploratory concepts to structured clinical practice, supported by increasing mechanistic understanding and accumulated clinical experience.

The fourth edition marked not only the consolidation of previous achievements but also the transition toward a new phase of maturity, characterized by greater awareness, more in-depth clinical questions, and an increasingly international perspective.

Recognizing the significance of this moment, the workshop was subtitled *"Are We at the End of the Beginning?"* This question reflects the collective consideration of the scientific community: after years of pioneering work in organ perfusion technologies and hemoadsorption, the field has reached a stage where fundamental principles have been established, early clinical evidence has emerged, and initial uncertainties have been partially resolved. At the same time, this progress has revealed new challenges that require more rigorous investigation, higher-quality evidence, and careful integration into clinical pathways. The workshop was therefore conceived as a forum to assess the current state of the field and define priorities for its future development.

Among these, extracorporeal blood purification therapies (EBPTs) have gained increasing importance in intensive care practice. Despite their growing use, uncertainties persist regarding optimal indications and timing.

Concurrently, transplant medicine has expanded donor eligibility criteria to include marginal organs from donation after circulatory death (DCD) and extended criteria donors (ECD). Research has therefore focused on advanced strategies for organ preservation and treatment aimed at maintaining viability, enabling functional assessment, and allowing targeted therapeutic interventions prior to transplantation.

The first day of the workshop was dedicated to dysregulated inflammatory diseases and extracorporeal purification therapies. Particular attention was given to the complex and dynamic role of inflammatory mediators—both pro-inflammatory and anti-inflammatory cytokines—in the pathophysiology of dysregulated inflammatory syndromes.

Clinical experiences were presented demonstrating that hemoadsorption and other purification techniques, including when combined with standard treatments such as antimicrobial therapy, may contribute to the control of inflammatory mediators and provide advanced hemodynamic support. Special attention was given to the possible interactions that may occur when these therapies are used together, for example, between extracorporeal purification techniques and medications such as antibiotics. Understanding these interactions requires a thorough knowledge of the underlying mechanisms.

Discussions addressed the application of extracorporeal therapies not only in septic shock but also in cardiac surgery and cardiogenic shock, highlighting the versatility of these approaches while emphasizing the need, across all clinical scenarios, for careful patient selection as well as appropriate dosing and timing of interventions.

The second day focused on organ preservation and regeneration in transplantation, as well as future perspectives, including xenotransplantation.

Sessions explored advances in *ex situ* organ management, including *in situ* and *ex situ* perfusion, and their role in improving transplant quality, expanding the donor pool, and enabling therapeutic interventions on the organ prior to implantation.

These scientific sessions were complemented by practical workshops that allowed participants to interact directly with perfusion technologies, promoting operational understanding and facilitating knowledge transfer from experienced centres to those adopting these techniques.

Discussions also addressed the current state of solid organ transplantation. Experts examined when and how to implement organ perfusion, how to tailor approaches to different organs and donor types, and how emerging data may influence clinical guidelines. Particular attention was devoted to temperature management in order to optimally prevent ischemia–reperfusion injury and thermal stress to the organ.

A critical evaluation was also dedicated to the influence of inflammatory mechanisms during both organ procurement and organ treatment phases, highlighting how organs are retrieved, preserved, perfused, and treated in an environment burdened by inflammatory mediators, thereby providing a strong rationale for integrating purification strategies into existing clinical workflows.

The workshop concluded with a forward-looking perspective, including the potential for personalized perfusion protocols, organ-directed targeted therapies, and closer integration between extracorporeal technologies and immunomodulatory strategies, with the awareness that perfusion will likely be required even in areas that now appear increasingly within reach, such as xenotransplantation.

A key theme throughout the workshop was the importance of generating robust scientific evidence, recognizing that the clinical experience of thousands of centres worldwide can provide valuable practical insights.

The program included 26 oral presentations, three practical sessions involving more than 200 participants, and 161 scientific contributions in poster format—original works collected in this supplement that represent the true innovative output of the Workshop.

These contributions covered a broad spectrum of experimental, translational, and clinical experiences, highlighting ongoing challenges.

The 161 scientific contributions published in this special issue of *Transplant International Journal* were systematically organized and classified according to specific thematic areas to facilitate consultation and enable pragmatic use of the content by clinicians and researchers.

This special issue is intended not only as a report of the workshop but also as a resource reflecting the current state of the art in purification therapies applied to transplantation and dysregulated inflammatory diseases.

In summary, the fourth Workshop on Purification Therapies, with 550 participants from around the world, promoted interdisciplinary dialogue and, by emphasizing evidence-based practice, contributed to the advancement of perfusion and purification therapies in modern medicine.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

Author MA is employed by the company Aferetica Srl.

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Program

Day 1 - Dysregulated Inflammatory Diseases, Extracorporeal Therapies
Friday, 19 September 2025

14:00 - 14:10	Welcome ***M. Atti***
14:10 - 14:30	Lecture - Cytokines: The Good? The Bad? How Much? *Chair: G. Grasselli* ***P. Pickkers***
14:30 - 16:00	Extracorporeal Therapies in Sepsis Three Years Later: Have we found the Philosopher's Stone? *Chairs: G. Castellano - V. M. Ranieri* Introductory Lecture ***J.L. Vincent*** Physiopathology of Sepsis and Extracorporeal Therapies ***C. Ince*** Real Life experiences ***G. Berlot*** Round Table
16:00 - 17:00	Poster Session *Chairs: F. Albrecht - S. Cattaneo - P. Esposito - M. Marengo - P. Raimondo - I. Riva - M. Thielmann - M. A. Valsecchi*
17:00 - 18:15	Extracorporeal Therapies and Antibiotic Therapies: To do: Yes, No or How? *Chairs: F. Aucella - I. Riva* Not To Do ***S. De Rosa*** To Do ***G. Bottari*** Round Table
18:15 - 18:45	Inflammation and Cardiac Surgery *Chairs: L. Potena* Influence on Intraoperative: the heart transplantation ***E. Nemeth*** Pre and Post-Operative management ***F. Pappalardo***
18:45 - 19:00	Closing of the day

Day 2 - Transplantation: From Conservation to Organ Regeneration
Saturday, 20 September 2025

PRE-MEETING "HANDS ON" SESSION - TECHNOLOGY FOR THE CLINICS

09:30 - 10:00

Introduction
Chair: M. Atti
A. Kurevija

Invited Lecture
L. Caneo

10:00 - 10:15

PerTravel
Chair: M. Boffini
S. Camagni

10:15 - 12:30

Hands on

1) PerLiver	2) PerKidney	3) PerLungs
Chair: P. Magistri	*Chair: Y. Luque*	*Chair: A. Palleschi*
R. Broere, E. Küçükerbil	***A. Amaduzzi, C. Carrara, F. Neri***	***A. Costamagna, M. Marro, E. Simonato***

13:30 - 14:10

Solid Organ Transplantation: The Present and The Future

Opening Lecture
Chair: L. De Carlis
G. Remuzzi

European State of Art
Chair: G.Feltrin
G. Oniscu

14:10 - 16:00

Perfusion: When, How, What's Next

When
Chairs: M. Fiorentino - G. Oniscu

a) Up-Front
A. Carraro
b) End-Ischemic
C. Puliatti

How
Chairs: P. Magistri - C. Quintini

a) Hypothermic
P. Dutkowski
b) Normothermic
R. Romagnoli
c) Sequential
R. J. Porte

Round Table
Chair: S. Nadalin

16:00 - 16:45 Poster Session
Chairs: M. A. Bongini - G. Castellano - D. Pagano - D. Pinelli - I. Scalera - Y. F. Suarez

16:45 - 17:00 What's Next

Long-Term Perfusion: What Potentials?
Chair: M. Spada
U. Cillo

17:00 - 18:45 Immunomodulation
Chairs: S. Lindstedt - S. Schneeberger

In-Situ
G. Feltrin
Ex-Situ

a) The Kidney
M. Fiorentino
b) The Liver
D. Ghinolfi - S. Schneeberger
c) The Lungs
M. Boffini

Round Table
Chair: U. Cillo

18:45 - 19:00 Closing & Final Remarque

Day 1 - Dysregulated Inflammatory Diseases, Extracorporeal Therapies

Overwhelming Inflammatory Disorders

A001

Microcirculation In Critically Ill Children With Septic Shock Undergoing Hemoadsorption

G. Bottari[1], V. Confalone[1], J. Creteur[2], C. Cecchetti[1] , F.S Taccone[2]

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Introduction

Sublingual microcirculation analysis has emerged as a valuable bedside technique for investigating the impact of septic shock on organ perfusion and assessing the efficacy of therapeutic interventions by directly visualizing microvascular blood flow.

Methods

This was a pre-planned secondary analysis of a Phase-II interventional single-arm pilot study conducted in the Pediatric Intensive Care Unit (PICU) at the Bambino Gesù Children's Hospital in Rome, Italy. We enrolled a total of 17 patients, with 13 meeting the criteria for inclusion with sublingual microcirculation monitoring. A CytoSorb adsorber was integrated into the CRRT circuit, and configured to operate in continuous veno-venous hemodiafiltration (CVVHDF) mode. Within the CRRT circuit, the CytoSorb cartridge was strategically positioned in series with the hemofilter, with routine replacement scheduled for every 24 h. This arrangement was sustained for a maximum duration of 96 h. Sublingual microcirculation assessments were conducted daily for five consecutive days starting from the initiation of blood purification. Several critical microcirculatory parameters were computed, including total small vessel density (TVD), proportion of perfused vessels (PPV), and perfused microvascular density (PVD).

Results

Thirteen patients were eligible to be investigated with sublingual microcirculation at baseline, 24, 48, 72 and 96 h from the onset of blood purification. Patients achieving a microvascular flow index (MFI) $\geq$ 2.5 and/or proportion of perfused

Table 1 | Median data of microcirculatory parameters for small vessels (<20 μm) of microvascular flow index (MFI) and proportion of perfused vessels (PPV) in responders and non-responders' patients at different time points. Baseline: before the onset of blood purification (BP); 24 h from the onset of BP (24 h); 48 h from the onset of BP (48 h); 72 h from the onset of BP (72 h); 96 h from the onset of BP (96 h)

MFIs AU (median)						
	Baseline	**24 h**	**48 h**	**72 h**	**96 h**	***p* value**
All	2.3	2.5	2.6	2.5	2.8	0.2
Responders	2.3	2.5	2.4	2.8	2.8	0.01
Non Responders	2.7	2.5	2.7	1.3	1.1	0.2
PPVs% (median)						
	Baseline	**24 h**	**48 h**	**72 h**	**96 h**	***p* value**
All	91	24.9	94.8	93.4	94.1	0.7
Responders	90	95	95	93	93	0.04
Non Resonders	93.2	96.4	98.8	62.5	54	0.4

vessels (PPV) exceeding 90% by 96 h were defined as responders. Among responders (10/13, 77%), a significant improvement in MFIs (p = 0.01) and PPVs% (p = 0.04) was noted between the baseline and 24 h from the end of treatment (see table 1).

Conclusion

In this pilot study, we have found a potential association between CytoSorb hemoadsorption and a microcirculation improvement in pediatric patients with septic shock, particularly when this observation has been associated with hemodynamic improvement.

A002

Pancreatic Stone Protein In The Diagnosis Of Sepsis In Children In PICU And Pediatric Emergency Department

G. Bottari[1], E. Paionni[2], D. Alunni Fegatelli[3], M. Murciano[4], F. Rosati[4 5], F. Ferrigno [4 5], M. Pisani[4], S. Cristaldi[4], A. Musolino[4], G. Borrelli[1], C. Bochicchio[1], L. Romani[6], M. De Luca[6], M. Agosta[7], L. Lancella[6], A. Villani[8], A. Vestri[9], M. Ciofi Degli Atti[10], C.F. Perno[7], O. Porzio [2], M. Raponi [11], C. Cecchetti [1]

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Introduction

Pancreatic stone protein (PSP) has recently emerged as a promising biomarker for the early detection of sepsis in both adults and pediatric populations. Early and accurate diagnosis is critical in pediatric sepsis, where clinical presentation may be nonspecific and delayed treatment can lead to poor outcomes.

Methods

In this prospective observational study, we enrolled 99 pediatric patients admitted to the intensive care unit (ICU) with clinical signs and symptoms consistent with systemic inflammatory response syndrome (SIRS), regardless of the presence of associated organ dysfunction. Eligible participants were aged between >1 month and <18 years. Blood levels of pancreatic stone protein (PSP) were measured within 24 hours of ICU admission using a nanofluidic point-of-care immunoassay (abioSCOPE®, Abionic SA, Switzerland).

Results

Patients with sepsis had significantly higher PSP levels compared to those with non-infectious systemic inflammation ($p < 0.001$). The optimal PSP cutoff value for diagnosing sepsis was determined to be 123 ng/mL, yielding a sensitivity of 0.63 (95% CI, 0.43–0.80) and a specificity of 0.89 (95% CI, 0.77–0.95). The area under the receiver operating characteristic curve (AUROC) for PSP was 0.82 (95% CI, 0.73–0.91), indicating good diagnostic performance. In comparison, the AUROCs for procalcitonin and C-reactive protein were 0.70 (95% CI, 0.58–0.82) and 0.72 (95% CI, 0.60–0.84), respectively (figure 1).

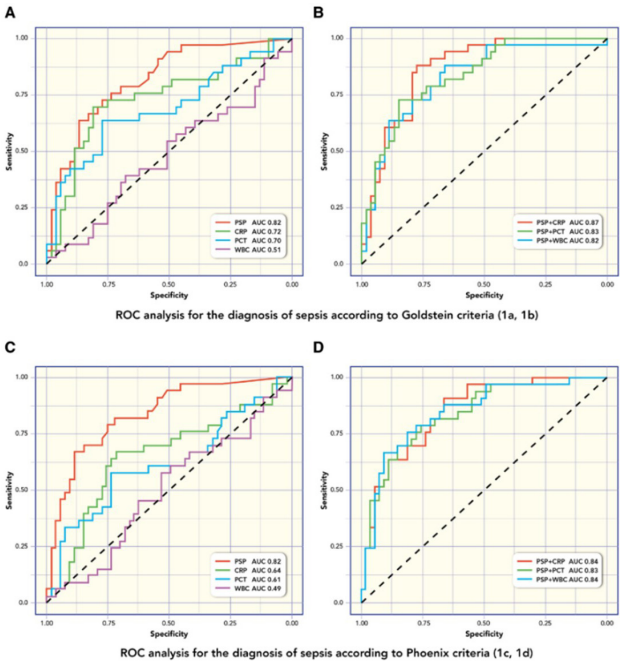

Figure 1 | **(A)**, Area under the receiver operating characteristic curve (AUROC) analysis of pancreatic stone protein (PSP), C-reactive protein (CRP), procalcitonin (PCT), and WBC for the diagnosis of sepsis (see Methods). **(B)** AUROC analysis of PSP plus PCT, PSP plus CRP, and PSP plus WBC for the diagnosis of sepsis. **(C)** AUROC analysis of PSP, CRP, PCT, and WBC for the diagnosis of sepsis according to the Phoenix criteria (see Methods). **(D)** AUROC analysis of PSP plus PCT, PSP plus CRP, and PSP plus WBC for the diagnosis of sepsis according to Phoenix criteria

Conclusion

Our findings support the potential utility of pancreatic stone protein (PSP) as a biomarker for the early diagnosis of sepsis. PSP demonstrated superior diagnostic performance compared to procalcitonin and C-reactive protein. However, due to residual diagnostic uncertainty associated with a positive PSP result, further studies are warranted—particularly those assessing PSP in combination with other established biomarkers—to better define its role in clinical decision-making.

A003

PSP (Pancreatic Stone Protein) As A Marker Of Infection And Index Of Effective Antibiotic Therapy

S. Perletti[3], A. Merli[2], G. Paolini[2], G. Gavanna[2], N. Gallina[4], A. Marino[1], T. Martino Valetti[1], I. Riva[1]

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Introduction

To date, there are few biomarkers routinely used during the management of patients with sepsis: C-reactive protein (CRP) and procalcitonin (PCT). The study aims to evaluate the Pancreatic Stone Protein (PSP) as a marker of response to antibiotic therapy and possibly to find a threshold value capable of guiding the timing of suspension of antimicrobial therapy.

Methods

The study is a prospective observational monocentric study involving patients with suspected sepsis/septic shock. PSP, CRP, PCT and IL-6 values were collected at enrollment (T0), on days 1 (T1), 3 (T3), 5 (T5) and 7 (T7) from enrollment.

Results

It can be seen (figure 1) how PSP tends to decrease during hospitalization in step with the improvement of the patient's clinical picture, PCR shows a late increase compared to the other markers. PSP seems to show statistically significant variations in T0-T1; T0-T3; T0-T5;

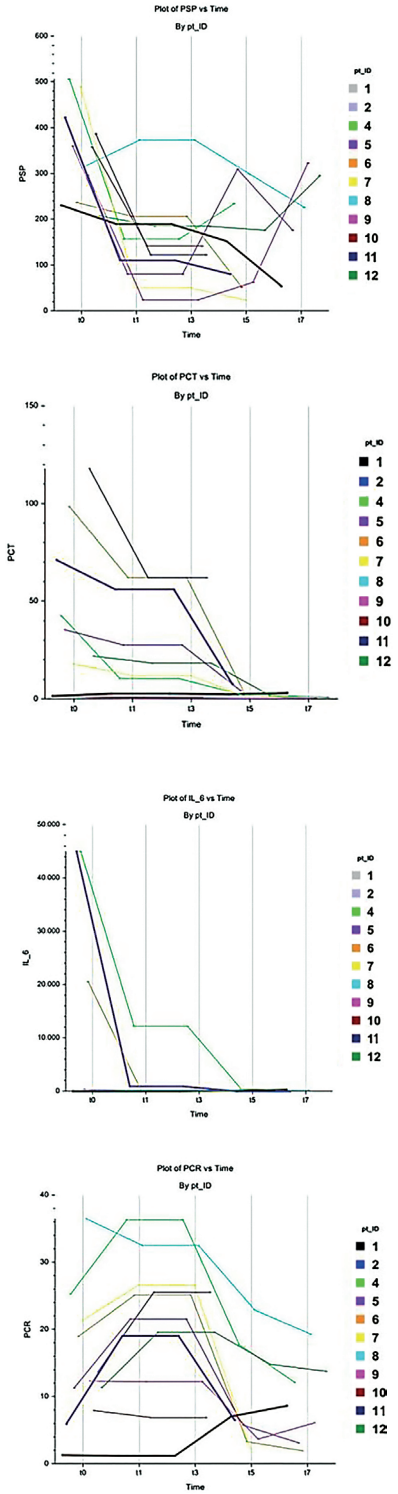

Figure 1 | Trend of PSP, PCT, IL6, CRP in single patients

T0-T7; T3-T7, just as PCT shows significant variations in T0-T7; T1-T5; T1-T7; T3- T5; T3-T7. The statistically significant difference in values regarding PSP between T0 and T1, T0 and T3, T0 and T5 could be due to the correct antibiotic therapy.

Conclusion

The trend of PSP and PCT in the population could reflect an earlier variation in PSP levels compared to the other markers taken into consideration, in particular PCT, which although showing significant variations, these are evident later than PSP. In general, a descending trend of PSP and PCT is noted which is reflected by the decreasing trend of SOFA and VIS and therefore by the clinical improvement of the patient. On the basis of these considerations, it is emphasized that PSP and PCT, alone or used in association, could play a useful role also in prognostic terms as well as clinical.

A004

Amount Of Blood Purified (ABP): Effects Of Cytosorb® On The Outcome Of Septic Shock Patients

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Introduction

Hemoadsorption has gained attention as a therapeutic approach in conditions like septic shock for removal of circulating inflammatory mediators from the bloodstream. Sepsis is characterized by a systemic inflammatory response, leading to the massive release of cytokines and other mediators that can cause organ dysfunction and tissue damage. By removing these harmful substances, hemoadsorption can help to mitigate the pathophysiological effects of sepsis.

Methods

We retrospectively evaluated 175 patients treated with CytoSorb®. The cause of septic shock was medical in 55%, surgical in 47% and undetermined in 5% of cases. Each sorbent was changed every 24 hours or less in case of clotting. The overall duration of the CytoSorb and the amount of blood purified (ABP) (Liters/kg of body weight) were considered as proxy of the intensity of treatment; this latter variable was calculated according to the formula: ABP = (D × BF)/BW, where D is the duration of treatment in minutes, BF is the blood flow in millilitres per minute, and BW is the actual body weight in kilograms.

Results

In the whole population, the distribution of ABP ranged from 0,39 to 50,40 l/kg BW; the ABP was significantly higher in Survivors than in Non Survivors (11,16 l/kg and 6,56 l/kg, respectively, p< 0,05). After plotting ABP against observed mortality, three different clusters were identified, including: Cluster A: Low ABP (<4 l/kg), n = 30; Cluster B: Intermediate ABP (4–9 l/kg), n = 56; Cluster C: High ABP (>9 l/kg), n = 86. For cluster C the mortality rate was significantly lower than the others (figure 1).

Conclusion

Our data indicates that CytoSorb® may be a valuable adjunctive therapy in the management of septic shock. We demonstrated a dose-effect relationship between the total amount of blood processed by CytoSorb® and mortality.

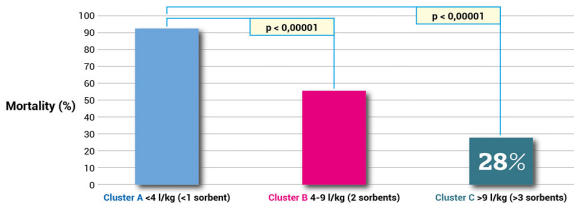

Figure 1 | Mortality rate in the different clusters

A005

Hemodynamic Improvement In Septic Shock Patients Treated With CytoSorb

G. Berlot [1], P. Carocci[1], V. Votrico[2], B. Iacoviello[1], N. Taverna[1], U. Gerini[3], V. di Maso[4], A. Tomasini [1]

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Introduction

While the Surviving Sepsis Campaign guidelines primarily focus on the management of sepsis with interventions like antibiotics, fluids, vasopressors, and organ support, the role of hemoadsorption and other similar therapies remains a topic of ongoing investigation. There are several extracorporeal devices and techniques currently used or under evaluation in sepsis management, including Cytokine adsorbers, devices that specifically target cytokines.

Methods

We retrospectively evaluated 175 septic shock patients treated with CytoSorb® admitted to our general ICU since 2016, July 1 till 2023 December 31. CytoSorb® was initiated within 24-48 hours from the onset of septic shock. The decision to continue the HA after the 2nd session was left to the attending team. Overall, 90 patients underwent ≥3 procedures and 85 patients underwent ≤ 2 sessions (high and low intensity group, respectively). The cause of septic shock was medical in 55%, surgical in 40% and undetermined in 5% of cases, respectively. For the entire population of patients, the admissions SAPS II score was 56. After the fluid resuscitation, an infusion of noradrenaline was started at an initial dose of 0,2 µg/kg/min and titrated in order to achieve a MAP ≥ 65 mmHg. The kidneys and the lung were the most involved organs; consequently, all patients were mechanically ventilated and the HA was associated with a CRRT.

Table 1 | Variables considered in all patients. Lactate (LAC), Procalcitonin (PCT), C-Reactive Protein (CRP), SOFA Score (Sequential Organ Failure Assessment Score), Noradrenaline (NA) and Mean Arterial Pressure (MAP)

Variable	All Patients		
	Pre-treatment	Post-treatment	P value
Lactate (U/l)	26,70 (15,55 - 52,50)	16,55 (6,60 - 42,18)	0,01445
PCT (ng/ml)	29,65 (5,16 - 82,80)	7,19 (2,29 - 26,83)	0,00002
CRP (mg/dl)	200 (119,58 - 285,98)	100,30 (48,20 - 186,90)	<0,00001
SOFA	12 (10 - 14)	11 (9 - 13)	0,00100
Noradrenaline (µg/Kg/min)	0,82 (050-1,07)	0,44 (0,11-0,91)	0,00001
MAP (mmHg)	63 (53,75-67,75)	67 (55,42-73,33)	0,00543

Results

We assessed variables as the time course of the SOFA score, procalcitonin (PCT), C-reactive protein (CPR), lactate, vasopressors and mean arterial pressure (MAP). In all patients, MAP significantly increased and lactate, PCT, CRP, SOFA score and the amount of noradrenaline administered significantly decreased at the end of the treatment as compared with the initial values (Table 1).

Conclusion

In septic shock patients, early and intense treatment with CytoSorb have shown overall hemodynamic improvement.

A006

Observed Vs Expected Mortality In Septic Shock Patients Treated With CytoSorb: A Real-World Scenario From Single Center Experience

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Introduction

Several studies have shown that the efficacy of hemoadsorption is highly dependent on key factors such as patient selection, timely initiation, and an adequate therapy duration. These factors are crucial because, when these parameters are met, patients typically experience noticeable hemodynamic improvement, including better circulation, stable blood pressure, and improved organ function. This improvement could, in turn, lead to a reduction in mortality rates, as the treatment helps address the underlying physiological disturbances that contribute to severe illness and death.

Methods

We retrospectively evaluated 175 patients treated with CytoSorb®. For the entire population the admissions SAPS II score was 56 (IQR 48-65); the SAPS II score of Non-Survivors (61, IQR 52-69) was significantly higher than in Survivors (53, IQR 45-59, p< 0,005). Overall, 86 patients died (49%) in ICU.

Results

The observed mortality (OM) was compared with the SAPS II-expected mortality (EM) either in the whole population of patients and in different subgroups (including early vs late starters, high vs low intensity patients, and early and high patients vs. late and low intensity patients); the OM was significantly lower than EM in the whole population (49% Vs 66% respectively; p=0,048), in high intensity patients (30% Vs 63%; p=0,002) and in early-starters/high intensity late starters (30% Vs 63%; p=0,02) (Table 1).

Table 1 | Observed versus expected mortality (%)

Categories	Expected Mortality (%)	Observed Mortality (%)	p
All (n=175)	66	49	0,048
Early Starters (n=102)	66	48	n.s.
Late Starters (n=73)	70	51	n.s.
High Intensity (n=90)	63	30	0,002
Low Intensity (n=85)	71	69	n.s.
Early starters-High Intensity (n=56)	63	30	0,02
Late Starters-Low Intensity (n=38)	74	68	n.s.

Conclusion

Mortality in all patients treated with Cytosorb has been significantly lower than expected based on the SAP II score. This reduction in mortality has been particularly pronounced in two patient groups: patients who received high-intensity hemoadsorption therapy; patients with the combination of starting therapy early and using high-intensity treatment. In summary, data from studies have confirmed that early initiation and high-intensity Cytosorb therapy are associated with significantly lower observed mortality compared to predictions, emphasizing the importance of prompt and aggressive treatment in critically ill patients.

A007

Hemodynamic Improvement In Septic Shock Patients Treated With CytoSorb: Subgroups Analysis

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Introduction

In septic patients undergoing hemoadsorption therapy, monitoring specific biomarkers and clinical parameters (noradrenaline, lactate, PCT, CRP, SOFA and MAP) is essential to assess the effectiveness of the treatment. These are all key markers that can help evaluate the efficacy of hemoadsorption. Improvement in these parameters typically suggests better circulatory, metabolic, and inflammatory control, pointing to a positive response

Table 1 | Changes of different variables subdivided according to the timing of initiation and the intensity of the treatment

Variable	Precocity median (IQR): Early Starters			Intensity median (IQR): High Intensity		
	Pre-treatment	Post-treatment	P value	Pre-treatment	Post-treatment	P value
Lactate (mg/dl)	31,8 (16,20-59,30)	17,05 (10,25 - 44,95)	0,02394	23,70 (15,40-40,90)	13,00 (7,60 - 24,50)	0,00230
PCT (ng/ml)	35,70 (6,18-99,25)	9,22 (2,65 - 37,95)	0,00076	29,90 (4,91-90,90)	3,14 (1,51 - 16,68)	0,00002
CRP (mg/dL)	196,40 (114,40-279)	102,65 (47,60 - 190,88)	0,00005	213,50 (127,50-319,20)	88,70 (43,10 - 186,70)	<0,000001
SOFA	12 (9,75-14)	10 (9 - 13)	0,03954	12 (10-14)	11 (9 - 13)	0,00977
Noradrenaline (µg/Kg/min)	0,76 (0,46-1,01)	0,4 (0,10-0,88)	0,00133	0,75 (0,48-10,3)	0,21 (0,06-0,53)	<0,000001
MAP (mmHg)	60 (53-65)	66,83 (50,75-77)	0,00843	63 (56,17-68)	69 (64,25-77,75)	<0,000001
Variable	**Precocity median (IQR): Late Starters**			**Intensity median (IQR): Low Intensity**		
	Pre-treatment	Post-treatment	P value	Pre-treatment	Post-treatment	P value
Lactate (U/l)	21,25 (14,48-41,08)	14,35 (8,88 - 42,45)	NS	31,90 (16,05-70,28)	26,50 (10,70 - 97,80)	NS
PCT (ng/ml)	17,40 (3,06-79,40)	3,40 (1,14 - 18,88)	0,00898	29,40 (5,36-81,00)	10,20 (3,14 - 32,81)	NS
CRP (mg/dL)	221,30 (132,40-352,25)	99,40 (48,35 - 184,15)	0,00021	181,20 (100,95-279,50)	112,90 (52,70 - 189,83)	0,00540
SOFA	12 (10-15)	11 (9 - 13)	0,01123	12 (9,50-15)	10,50 (9 - 13)	NS
Noradrenaline (µg/Kg/min)	0,83 (0,50-1,13)	0,48 (0,10-0,92)	0,00236	0,9 (0,51-1,12)	0,86 (0,36-1,20)	NS
MAP (mmHg)	63 (60-70)	67 (57-73,33)	NS	60 (53-67)	60 (45,42-70)	NS

to therapy. Tracking these markers together allows for a comprehensive assessment of whether hemoadsorption is contributing positively to the patient's recovery from sepsis.

Methods

We retrospectively evaluated 175 septic shock patients treated with CytoSorb® admitted to our general ICU since 2016, July 1 till 2023 December 31. CytoSorb® was initiated within 24-48 hours from the onset of septic shock. The decision to continue the HA after the 2nd session was left to the attending team. Overall, 90 patients underwent ≥3 procedures and 85 patients underwent ≤ 2 sessions (high and low intensity group, respectively). The cause of septic shock was medical in 55%, surgical in 40% and undetermined in 5% of cases, respectively.

Results

We assessed variables as the time course of the SOFA score, procalcitonin (PCT), C-reactive protein (CPR), lactate, vasopressors and mean arterial pressure (MAP). In all patients, MAP significantly increased and lactate, PCT, CRP, SOFA score and the amount of noradrenaline administered significantly decreased at the end of the treatment as compared with the initial values. When the same variables were compared by subdividing the patients according to the timing and the intensity of the treatment, it appeared that these variations were more marked in more intensely treated early starters (Table 1 of the supplementary material (Table 1).

Conclusion

In septic shock patients, treatment with CytoSorb results in hemodynamic and clinical improvement, particularly in early and intense treated patients.

A008

Stercoral Peritonitis Leading To Septic Shock: Successful Use Of Adjunctive Hemoadsorption In A Critically Ill Patient

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Introduction

Stercoral peritonitis is a life-threatening consequence of stercoral colitis, resulting from colonic perforation due to fecal impaction and pressure-induced necrosis. Without prompt intervention, this condition can rapidly escalate to septic shock and fatal multi-organ failure.

Methods

A 64-year-old female patient underwent exploratory laparotomy for acute intestinal obstruction. Intraoperatively, stercoraceous peritonitis was identified, secondary to colonic perforation from fecal impaction. Postoperatively, the patient developed severe septic shock, complicated by acute kidney injury and respiratory failure. Laboratory evaluation revealed elevated serum creatinine (3.4 mg/dL), a lactate level >3 mmol/L, a 256 mmHg P/F ratio and a near-normal blood pH of 7.38. She remained profoundly hemodynamically unstable, requiring high-dose vasopressor support to maintain adequate perfusion. Broad-spectrum antimicrobial therapy with meropenem and a combination of piperacillin-tazobactam was promptly initiated. Due to persistent septic shock and multi-organ dysfunction, the patient underwent two sessions of hemoperfusion using Toraymyxin (PMX-DHP) for endotoxin removal. Given the ongoing inflammatory response and hemodynamic instability, CytoSorb therapy was initiated and lasted 24 hours. The next day, a second CytoSorb session followed as part of extracorporeal blood purification to further reduce circulating inflammatory mediators.

Results

Despite initial aggressive resuscitation and supportive measures, the patient remained in critical condition, underscoring the complexity of sepsis-related multi-organ failure. The use of extracorporeal therapies contributed to a progressive improvement in hemodynamic stability (see Figure 1), allowing time for antimicrobial therapy to take effect. Over the following days, the patient's condition gradually improved; she became alert and clinically more stable. She was subsequently transferred in stable condition to the surgical department for continued management and follow-up care.

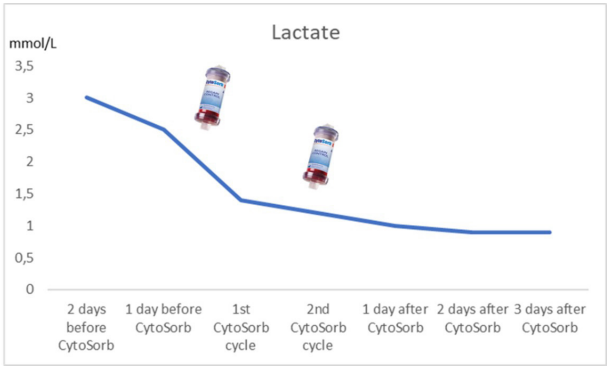

Figure 1 | Lactate trend over CytoSorb treatment period

Conclusion

The integration of extracorporeal purification was associated with gradual hemodynamic improvement. This may have played a key role in controlling the overwhelming cytokine storm, bridging the critical period until the antimicrobial therapy could exert its full effect.

A009

Clozapine-Induced Rhabdomyolysis And AKI: The Role Of Hemoadsorption (Cytosorb® Adsorber)

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Background

Rhabdomyolysis is an important muscle cell injury which may induce an acute kidney injury (AKI). Clozapine has been associated with rhabdomyolysis, although this association remains poorly understood and underestimated.

Methods

A 43-year-old man went to the Emergency Room for dyspnea and hyperpyrexia. The medical history revealed a state of schizophrenia, a recent hospitalization for pulmonary aspergillosis treated with fluconazole and normal renal function. The patient was positive for COVID-19 test and had pulmonary thickening on the chest x-ray. He developed lung failure, so he was transferred to the Intensive Care Unit where he started ventilator support. Lab tests revealed a worsening of renal function (sCr 6.05 mg/dl, BUN 170 mg/dl), anemia, hyperphosphatemia, thrombocytopenia, elevated levels of myoglobin and CK. Clozapine was stopped following the diagnosis of rhabdomyolysis. A reduced urine excretion appeared. We decided to start Cytosorb® treatment in combination with CRRT (CVVHDF). Cytosorb® was stopped a day later (three sessions for a total treatment time of 24 hours).

Results

Within 12 hours, myoglobin levels decreased from 12,000 to 8,237 ng/ml while at the end of the treatment there was a reduction of 68.65%. It has also been observed a reduction of CK levels over 12 hours from 101,380 to 28,463 U/l and at the end of the treatment the reduction rate was 92.29% (Fig.1). During the next days, parameters of renal function, CK and myoglobin decreased in association with an increased patient's urine output and ventilator support was diminished. The patient's condition improved subsequently and renal function completely recovered.

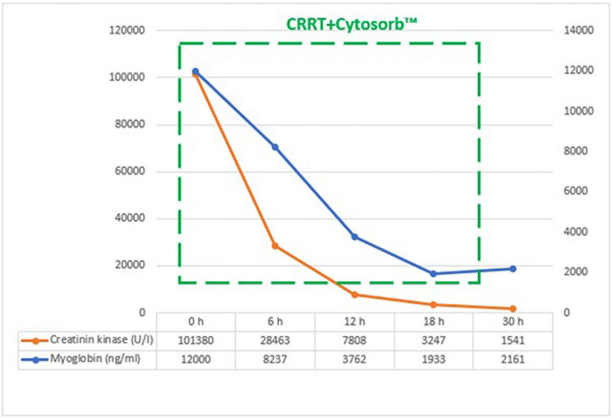

Figure 1 | Myoglobin and CK levels over 30 hours

Conclusion

We observed a high decrease of myolysis indices after application of Cytosorb® cartridge followed by an improvement of renal function. Thus, in our opinion Cytosorb® should be considered in case of rhabdomyolysis drug-induced not only for the treatment but also in the prevention of AKI.

A010

Use Of The Cytosorb Device In Hemodynamic Control Following Subarachnoid Hemorrhage: A Case Report

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Introduction

Subarachnoid hemorrhage (SAH) is an acute neurological condition associated with high mortality and morbidity. The systemic inflammatory response it triggers may contribute to severe complications such as vasospasm, cerebral edema, and septic shock. In the postoperative setting, managing hemodynamic instability secondary to SAH can be particularly challenging.

Early initiation of extracorporeal support therapies such as Continuous Renal Replacement Therapy (CRRT) combined with CytoSorb®—the only hemoadsorption cartridge certified for the removal of cytokines, bilirubin, myoglobin, Ticagrelor, and Rivaroxaban from whole blood—allows timely control of the inflammatory and toxic burden, with potential improvement

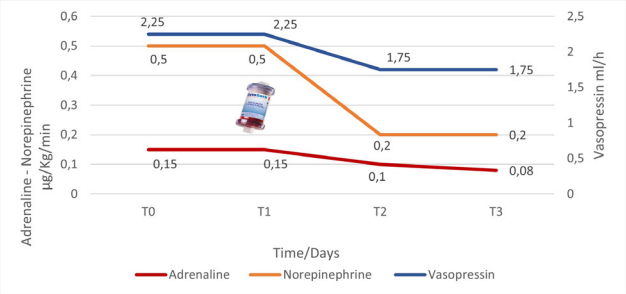

Figure 1 | Vasopressors trend before and after use of CytoSorb

in both hemodynamic and neurological parameters. This strategy may help prevent progression toward multiple organ dysfunction, significantly improving the prognosis of neurocritical patients.

Methods

A 71-year-old patient developed hemodynamic instability following postoperative subarachnoid hemorrhage. In the intensive care unit, he received catecholamine support with adrenaline at 0.15 µg/kg/min, norepinephrine at 0.5 µg/kg/min, and vasopressin at 2.25 U/h. Due to clinical refractoriness and the suspected contribution of pro-inflammatory mediators, CytoSorb® therapy was initiated in combination with continuous veno-venous hemodiafiltration (CRRT). The device was used for 24 hours.

Results

After the first 24 hours of CytoSorb® treatment, adrenaline dosage decreased from 0.15 to 0.10 µg/kg/min and norepinephrine from 0.5 to 0.20 µg/kg/min. Vasopressin was reduced to 1.75 U/h. After an additional 24 hours, adrenaline further declined to 0.08 µg/kg/min, while norepinephrine remained stable at 0.20 µg/kg/min (Figure 1). Blood pressure parameters remained stable throughout the treatment, allowing for a progressive reduction in vasopressor requirements without signs of hypoperfusion.

Conclusion

The use of the CytoSorb® device contributed to a rapid improvement in the hemodynamic profile of an elderly patient with post-subarachnoid hemorrhage instability. The progressive reduction in vasopressor requirements suggests effective modulation of excessive pro-inflammatory mediators, supporting the management of systemic inflammation and/or refractory shock.

A011

CytoSorb® Hemoadsorption In A Complex Case Of Rhabdomyolysis And Hemorrhagic Shock: Role In Kidney Function Restoration

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Introduction

Rhabdomyolysis is a significant cause of acute kidney injury (AKI) in critically ill patients, often resulting from trauma, sepsis, surgery, or prolonged ischemia. The release of myoglobin into circulation contributes to renal damage through tubular toxicity and vasoconstriction. Standard continuous renal replacement therapy (CRRT) is limited in myoglobin clearance due to its size and hydrophobic properties. CytoSorb® hemoperfusion has emerged as a promising adjunct for early myoglobin removal to prevent or mitigate AKI.

Methods

A 17-year-old female was admitted in critical condition following a high-impact road accident. She presented with hemorrhagic shock (BP 95/55 mmHg, HR 116 bpm), metabolic alkalosis, elevated lactate (4.4 mmol/L), and severe hyperkalemia (6.75 mmol/L). Imaging revealed multiple fractures, including a severe pelvic injury and soft tissue trauma in the perineal region. After surgical stabilization and ICU admission, she received mechanical ventilation, vasopressors, and fluid resuscitation.

Results

Within 24 hours, the patient developed oliguria (<30 mL/h) and myoglobin levels exceeded 10,000 ng/mL.

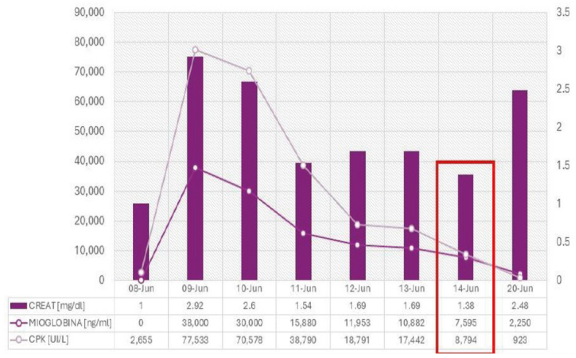

Figure 1 | Trend of serum myoglobin and CPK levels and renal function during CytoSorb treatment

Serum creatinine doubled, meeting criteria for KDIGO stage III AKI. CRRT combined with CytoSorb® hemoperfusion was initiated, with cartridges replaced every 24 hours for four days. A significant reduction in myoglobin occurred within 48 hours, and renal function gradually improved. Renal replacement therapy was discontinued by day 12, with full renal recovery by day 30 (Fig.1). No further dialysis was needed.

Conclusion

This case underscores the potential benefit of CytoSorb® hemoperfusion in managing rhabdomyolysis-associated AKI. Initiating treatment early, particularly in patients with myoglobin >10,000 ng/mL, may enhance renal recovery. While supportive care remains essential, adjunctive hemoadsorption may offer a valuable strategy in complex trauma-induced AKI. Prospective studies are warranted to refine treatment timing and patient selection.

A012

Impact Of CytoSorb On Outcomes In Septic Shock Patients: A Propensity Score Matching Study

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Introduction

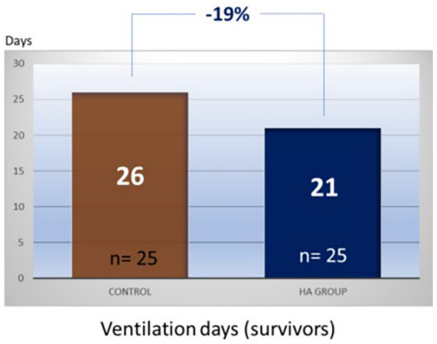
Evolution of sepsis treatment recognizes that sepsis is not just an infection but also a complex dysregulated immune response that can lead to widespread inflammation, organ dysfunction, and even death.

Methods

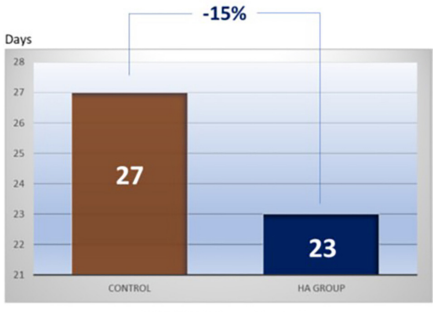
We retrospectively evaluated the use of CytoSorb® in the treatment of septic shock and compared it to a historical cohort of patients treated with Standard of Care (SoC) therapy as per the Surviving Sepsis Campaign guidelines. The study reviewed 29 patients treated with CytoSorb®. These patients received: Day 1: Two 12-hour sessions of CytoSorb®; Day 2: One 24-hour session of CytoSorb®. The outcomes of the CytoSorb® group were compared to those of a historical Control Group of 130 septic shock patients. To ensure that the two groups (CytoSorb® and SoC) were comparable, a propensity score matching was performed. After matching, a final comparison was made between: CytoSorb® group: 25 patients; Control group: 25 patients from the historical cohort.

Results

The Cytosorb group showed a significant reduction in lactate levels (2.2 mmol/l) compared to the control group (5 mmol/l), with a p-value of 0.026. Furthermore, the Cytosorb group had 19% fewer ventilation days (21 days)



Ventilation days (survivors)



LOS-ICU (survivors)

Figure 1 | Ventilation days and LOS-ICU for Control group compared to the Cytosorb group

compared to the control group (26 days). There was a 15% reduction in ICU length of stay for the Cytosorb group (23 days) compared to the control group (27 days) (figure 1). In addition to that, in a subgroup of 17 patients in the Cytosorb group, there was a notable reduction in markers of inflammation: a decrease in IL-6, from 4,590 pg/ml to 280 pg/ml (p=0.00053), a significant reduction in PCT, from 66.50 ng/ml to 29.00 ng/ml (p=0.00017), further supporting the anti-inflammatory effect of Cytosorb.

Conclusion

These findings suggest that Cytosorb may offer benefits in managing critical illness, particularly through its impact on metabolic balance, inflammation, and overall recovery in the ICU setting.

A013

Impact Of CytoSorb On Mortality In Septic Shock Patients: A Propensity Score Matching Study

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[1] Anesthesia and Intensive Care, San Giuseppe Hospital, Empoli, Italy

Introduction

The evolution of sepsis and septic shock treatment over recent years emphasizes a shift in focus from solely targeting the pathogen to also addressing the host's immune-inflammatory response. One of the proposed treatments involves using adsorptive devices or therapies that reduce circulating cytokines to prevent or mitigate systemic inflammation.

Methods

We retrospectively evaluated the use of CytoSorb® in the treatment of septic shock and compared it to a historical cohort of patients treated with Standard of Care (SoC) therapy as per the Surviving Sepsis Campaign guidelines. The study reviewed 29 patients treated with CytoSorb®. These patients received: Day 1: Two 12-hour sessions of CytoSorb®; Day 2: One 24-hour session of CytoSorb®. The outcomes of the CytoSorb® group were compared to those of a historical Control Group of 130 septic shock patients. To ensure that the two groups (CytoSorb® and SoC) were comparable, a propensity score matching was performed. After matching, a final comparison was made between: CytoSorb® group: 25 patients; Control group: 25 patients from the historical cohort.

Results

ICU Mortality: The CytoSorb® group had a lower ICU mortality (40%) compared to the control group (64%), though this result did not reach statistical significance (p=0.089), suggesting a trend toward improved survival with CytoSorb®. Observed vs Expected Mortality: The observed mortality in the CytoSorb® group was much lower than the expected mortality based on SAPS II (72%), indicating a favourable impact of CytoSorb® on survival. 28-Day Hospital Mortality. There was a significant reduction in 28-day hospital mortality in the CytoSorb® group (44% vs. 72%, p=0.045), providing compelling evidence that CytoSorb® treatment can improve short-term survival in septic shock (Figure 1).

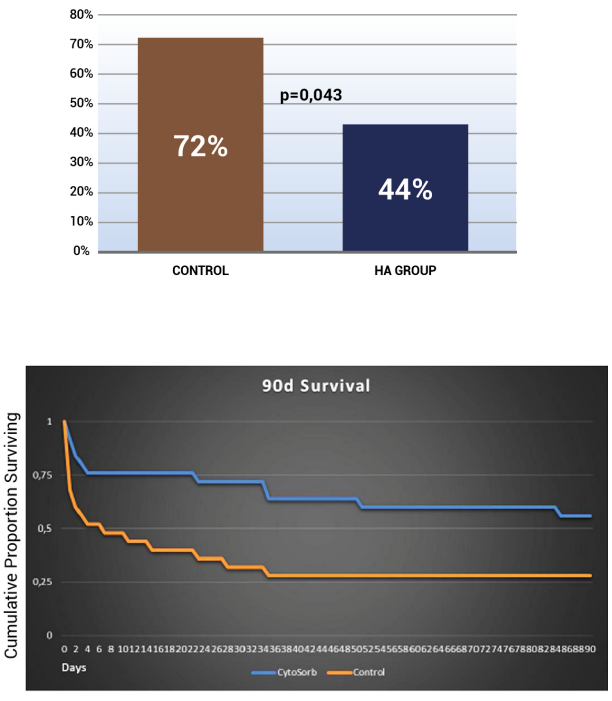

Figure 1 | Hospital mortality and survival analysis by Kaplan-Meyer curves

Conclusion

CytoSorb® in septic shock patients may have a positive impact on mortality rates, particularly in terms of both ICU mortality and 28-day hospital mortality.

A014

Use Of Extracorporeal Blood Purification Therapies Including CytoSorb On Acute Myeloid Leukemia (AML) Patients With Sepsis

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Introduction

This is a brief case series evaluating the use of CytoSorb® therapy in the management of sepsis in patients with acute myeloid leukemia (AML). The treatment of acute myeloid leukemia (AML) requires careful management, especially when complicated by sepsis. Sepsis in these patients can be managed with various approaches, one of which includes ExtraCorporeal Blood Purification Therapies (EBPTs).

Methods

The study retrospectively analyzed the use of CytoSorb® (an EBPT) in six AML patients who were septic. The specific protocol included a combination of therapies: LPS (lipopolysaccharide) adsorbers, CytoSorb, and continuous renal replacement therapy (CRRT).

Results

After sequential therapy, several clinical markers showed improvement (see figure 1):

- **Procalcitonin (PCT)**, a marker of sepsis, decreased from 7.68 ng/ml (before therapy) to 1.28 ng/ml (after therapy).

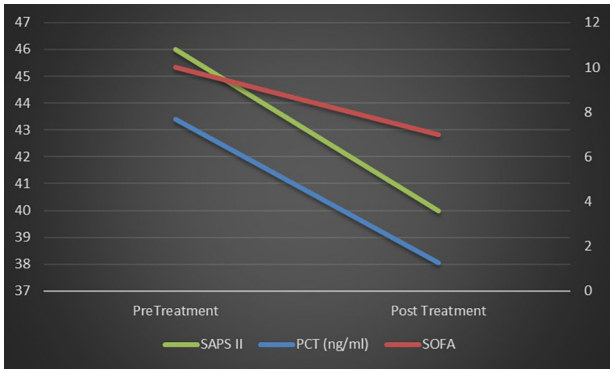

Figure 1 | (PCT, SOFA, SAPS II score pre and post treatment)

- **SOFA (Sequential Organ Failure Assessment)** score, which indicates organ dysfunction, improved from 10 to 7.
- **SAPS II (Simplified Acute Physiology Score)**, a scoring system to assess the severity of disease, also showed improvement from 46 to 40.

Mortality in the cohort was 33%, which was lower than the expected mortality rate of 45% based on the patients' severity (SOFA and SAPS II score).

Conclusion

This study represents one of the first case series exploring the potential benefits of EBPT, particularly CytoSorb, in treating sepsis in AML patients. While the results are promising, additional research is needed to confirm these findings and further evaluate the efficacy of this approach.

A015

Use Of CytoSorb And CKRT In Burn Patients With Septic Shock And Acute Kidney Injury

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Introduction

The use of continuous kidney replacement therapy (CKRT) is critical in burn patients suffering from Acute Kidney Injury (AKI), particularly for managing fluid overload and electrolyte imbalances. However, CKRT doesn't directly address the underlying inflammatory response that exacerbates the patient's condition in AKI-associated septic shock. Sorbent therapies, such as cytokine adsorbers, are an emerging approach that could potentially help manage these metabolic and inflammatory derangements.

Methods

Out of 461 admitted burn patients between January 2017 and December 2022, 35 developed AKI-associated septic shock receiving CKRT for more than 72 h. Among them, 11 patients were treated with CytoSorb as adjunctive therapy for refractory septic shock and 24 patients were not. CKRT was started when patients were in a trend of fluid overload and not responsive to conservative management. CytoSorb and CKRT were coupled in all patients of the Sorbent group. CytoSorb was changed after 24 h, as well as the extracorporeal circuit.

Results

No significant difference was found between the 2 groups for age, burn size, SOFA score, lactate, norepinephrine, and expected mortality by the Baux index (54.0 and 55.1%, respectively). Patients in the Sorbent group required significantly less norepinephrine compared to those in the Control group, indicating a potential improvement in hemodynamic stability (Fig. 1). This effect was observed over the first four days of treatment. In-hospital mortality rate was 45.4% for the Sorbent group and 70.8% for the Control group, showing a notable improvement in survival among those who received CytoSorb. Kaplan-Meier Survival Analysis at 270 days demonstrated a significant improvement in survival for the Sorbent group ($p = 0.0445$). In both groups, all surviving patients had recovered renal function by discharge, while no non-survivors did.

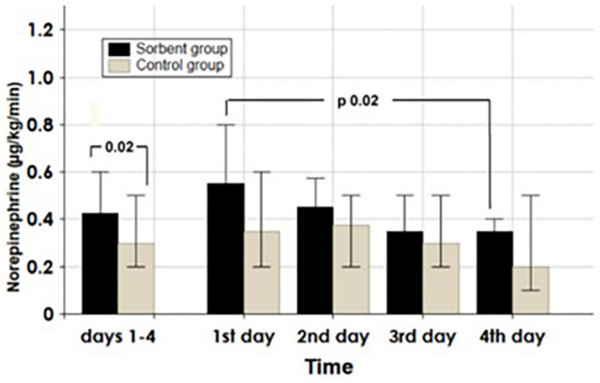

Figure 1 | Outcome of norepinephrine requirement in the first 4 days for Sorbent (n 11 patients) and Control groups (n 24 patients). A significant difference was found between the norepinephrine requirement of days 1–4 and between day 1 and day 4 for patients of the Sorbent group. Data were given as median with quartiles (25th and 75th percentiles). $p > 0.05$ with Kruskal-Wallis ANOVA and multi-comparison test

Conclusion

This finding supports that CytoSorb could be a valuable adjunct in the treatment of septic shock and AKI in burn patients. The combination of CKRT and CytoSorb might enhance clinical outcomes and reduce mortality.

A016

Sepsis From Stercoral Peritonitis: Surgical And Hemoadsorptive Management

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Introduction

Stercoral peritonitis is a severe inflammation of the peritoneum caused by the leakage of fecal material

into the abdominal cavity, usually following a perforation of the gastrointestinal tract—most commonly the colon.

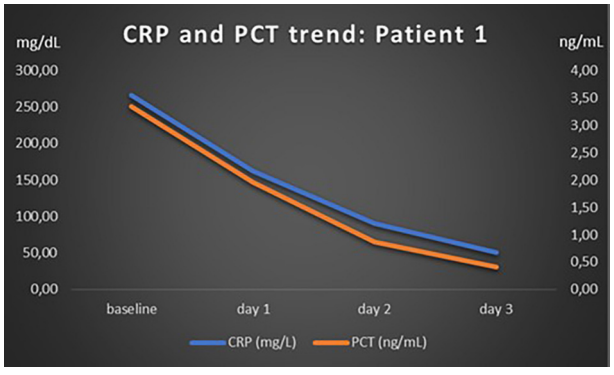
Methods

We report the case of 2 patients who developed sepsis due to stercoral peritonitis. **Patient 1**: stercoral peritonitis secondary to diastatic rupture of the cecum. Intraoperatively, vascular compromise of the right and transverse colon was observed. A fixed neoplastic obstruction involving the left colonic flexure, mesocolon, pancreas, and spleen was identified. The diagnostic workup included contrast-enhanced total-body CT, ECG, blood tests, and tumor markers. The patient received two units of packed red blood cells prior to surgery. An emergency exploratory laparotomy was performed, including peritoneal lavage, extended right hemicolectomy, peritoneal biopsies, and creation of a protective ileostomy. **Patient 2**: stercoral peritonitis caused by perforation of a neoplastic lesion in the sigmoid colon. Associated findings included hepatic metastases and cerebellar ischemia. An emergency laparotomy was performed, involving thorough peritoneal lavage, resection of the perforated sigmoid segment, and creation of a left-sided colostomy. The procedure aimed to control the source of infection and prevent further peritoneal contamination. The case highlights the complexity of managing abdominal sepsis in the context of advanced malignancy.

Due to elevated inflammatory markers (CRP and PCT), renal and liver impairment, both patients underwent continuous renal replacement therapy for 3 days and 2 or 3 consecutive 24-hour sessions of CytoSorb hemoadsorption.

Results

Following days of CytoSorb therapy, liver function improved (reduced bilirubin, increased cholinesterase, improved AST levels). Inflammatory markers decreased markedly (see figure 1). Both patients had an uneventful postoperative course and was discharged in stable condition.



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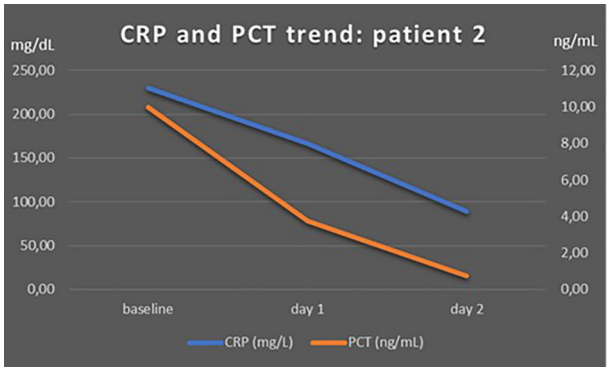

Figure 1 | CRP and PCT trend over CytoSorb treatment in ICU

Conclusion

CytoSorb proved effective in reducing systemic inflammation in two cases of sepsis due to stercoral peritonitis, supporting its role as adjunctive therapy in severe abdominal sepsis.

A017

Use Of CytoSorb In Severe Hypoxemic Acute Respiratory Failure From Drug Abuse

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Introduction

Comatose state with severe hypoxemic acute respiratory failure from drug abuse is life-threatening. Depressed respiratory drive and impaired alveolar ventilation lead to critical hypoxemia. Immediate airway management, ventilatory support, and intensive monitoring are essential to prevent irreversible brain injury, organ failure, and improve chances of recovery in these patients.

Methods

The patient arrived at the emergency department in a comatose state with severe hypoxemic acute respiratory failure secondary to drug abuse. Initial management included orotracheal intubation and invasive mechanical ventilation, followed by non-invasive ventilation and high-flow nasal cannula therapy. Imaging revealed a bronchopneumonic focus in the left lung with associated pleural effusion, complicated by superinfection with Klebsiella pneumoniae and Proteus mirabilis. Additionally, the patient developed acute anemia and acute renal failure. As a result, he underwent four cycles of continuous veno-venous hemodiafiltration (CVVHD) combined with CytoSorb therapy (4 CytoSorb changed every 12 hours) to support renal function and modulate the inflammatory response.

Results

The patient was transferred from the intensive care unit to the Respiratory Diseases Department in stable and clearly improving condition. The pleural effusion showed advanced resolution, accompanied by progressive improvement in key clinical parameters, including the P/F ratio, mean arterial pressure (MAP), serum creatinine levels, and overall renal function.

Conclusion

Dialysis combined with CytoSorb therapy, administered at appropriate frequency and dosage, represents an effective therapeutic option for patients with severe hypoxemic acute respiratory failure due to drug abuse. This approach supports renal function and helps control the systemic inflammatory response, contributing to overall clinical stabilization and improved patient outcomes.

A018

Adjunctive CytoSorb® Hemoadsorption In H1N1-Related Respiratory Failure

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Introduction

H1N1 virus is a significant cause of respiratory infections, capable of progressing to severe viral pneumonia and acute respiratory distress syndrome (ARDS) in vulnerable populations. In critical cases, the host immune response may trigger a hyperinflammatory state, contributing to respiratory failure and multiorgan dysfunction. CytoSorb®, an extracorporeal cytokine hemoadsorption device, has emerged as a potential adjunctive treatment in critically ill patients experiencing systemic inflammation. By reducing circulating levels of pro-inflammatory cytokines, CytoSorb® aims to restore immune homeostasis and improve organ function.

Methods

We report the case of a 49-year-old patient admitted for H1N1 virus positivity and acute respiratory failure (P/F 84 mmHg). The patient required invasive mechanical ventilation and developed hyperinflammation, associated with hemodynamic instability (Norepinephrine 0.2 mcg/kg). CytoSorb® treatment combined with continuous veno-venous hemodialysis (CVVHDF) was administered, with three cartridges in two days, which led to stop the administration of vasopressors. Three days later, due to respiratory worsening (P/F 60 mmHg, and pronation necessity), a second cycle of CVVHDF plus CytoSorb® was started, for two days.

Results

During the first cycle, the patient showed respiratory recovery with haemodynamic stabilization (stop of norepinephrine on the first day), allowing the patient to recovery from pronation. On second cycle, patient showed a gradual reduction of cytokines and inflammatory markers (IL-6 from 86.5 pg/mL to <2 pg/mL; PCR from 12.2 mg/L to 2.99 mg/L), sign that hemadsorption therapy was working, concomitant with White Blood Cells decrease. gradual weaning from mechanical ventilation and transfer to the medical ward.

Conclusions

The second cycle of CytoSorb® treatment was necessary due to respiratory deterioration after the first cycle, suggesting that in some patients with severe H1N1 virus and persistent hyperinflammation, multiple hemoadsorption sessions may be required to achieve effective modulation of the inflammatory response.

In this case, CytoSorb® proved to be a valuable and well-tolerated adjunctive therapy, contributing to a clear clinical and biochemical improvement. Its use supported the resolution of the hyperinflammatory state and the recovery of respiratory function. These observations reinforce the potential role of CytoSorb® in the management of critically ill H1N1 patients, particularly when conventional therapy alone is insufficient to control inflammation.

A019

Use Of CytoSorb® Hemoadsorption For Rhabdomyolysis And Inflammatory Modulation Following Trauma And Acute Appendicitis: A Case Report

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Introduction

CytoSorb® hemoadsorption has emerged as an adjunctive therapy in critical care for the removal of middle molecular weight substances such as myoglobin and cytokines. Its dual action makes it particularly valuable in complex cases involving multiple aetiologies. Rhabdomyolysis, often due to traumatic muscle injury, may lead to acute kidney injury (AKI) via direct nephrotoxicity of circulating myoglobin. In parallel, conditions such as sepsis or severe infection—like acute appendicitis—can trigger a systemic inflammatory response, contributing to hemodynamic instability and multi-organ dysfunction. Although unrelated in etiology, trauma-induced rhabdomyolysis and appendicitis-related sepsis may coexist and synergistically worsen the clinical picture. In such settings, extracorporeal blood purification with CytoSorb® integrated into continuous renal replacement therapy (CRRT) may help control both muscle breakdown products and systemic inflammation.

Methods

A 54-year-old male was admitted to the ICU, for clinical deterioration after a pelvic fracture sustained in an accidental fall. During hospitalization, he developed acute abdominal pain; CT revealed appendicitis, and urgent laparoscopic appendectomy was performed. Due to rising serum myoglobin and worsening inflammatory markers, CRRT was initiated with an Oxiris® filter and three sequential CytoSorb® cartridges over 72 hours. Laboratory parameters (IL-6, PCT, CPK, myoglobin) were monitored throughout.

Results

Following initiation of hemoadsorption, serum myoglobin decreased from 1058 ng/mL to 163 ng/mL, IL-6 peaked at 803.3 pg/mL and dropped to 14.3 pg/mL, while PCT fell from 66.8 to 37.31 ng/mL. CPK decreased from 662 U/L to 99 U/L (figure 1). Clinical improvement included resumption of spontaneous diuresis and progressive reduction in vasopressor requirements. No further CRRT sessions were needed.

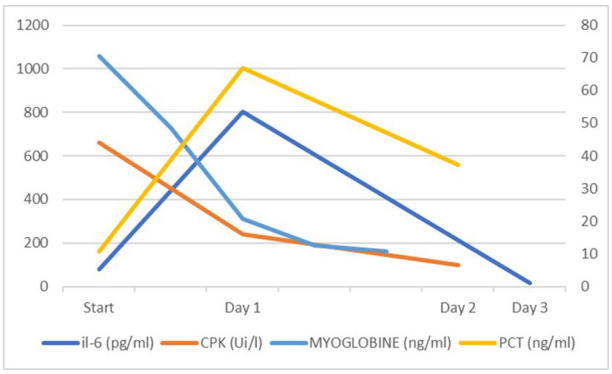

Figure 1 | Labs trend during hemadsorption therapy

Conclusions

This case highlights the utility of CytoSorb® hemoadsorption in managing two distinct but coexisting pathophysiological processes: rhabdomyolysis-induced AKI and sepsis-driven inflammation. The combined biochemical and clinical response supports the integration of CytoSorb® into CRRT for patients with multifactorial critical illness.

A020

Capnocytophaga Canimorsus Zoonosis: Early Treatment With Cytosorb

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Introduction

Capnocytophaga canimorsus is a Gram-negative bacillus present in pets. Identifying the germ is challenging and manifestations could be severe if contracted by humans.

Methods

In the case we describe the application of hemadsorption to mitigate the sepsis caused by Capnocytophaga canimorsus.

Case Presentation

A 63-year-old woman was admitted to the emergency department with a hypotensive state, fever, profuse diarrhoea, and diffuse pain. Blood tests indicated pancytopenia, thrombocytopenia, and renal failure. Her creatine phosphokinase (CPK) was 1597 U/L, C-reactive protein (CRP) was 17.22 mg/dL, and troponin was 95 pg/mL. Emogas revealed lactates at 9.1 mmol/L. The patient required noradrenaline at 0.16 mcg/kg/min.

Diagnostic procedures included blood cultures, urine culture, swabs, and stool culture.

On Day 2, conditions worsened, necessitating an increase of noradrenaline, initiation of Empressin, and non-invasive ventilation. pH was 7.51, lactates 9.6 mmol/l, procalcitonin (PCT) 96 ng/ml.

By Day 3, further elevations in inflammatory markers (PCT 100 ng/ml, CRP 19 mg/dL) and troponin (22925 pg/mL) and high lactates (5.5 mmol/L) prompted the start of continuous venovenous hemofiltration with Cytosorb, with no anticoagulation, to address the inflammatory response. After 12 hours, the sorbent was changed, with improved hemodynamics and a decrease in vasoactive drugs requirements (NA 0.08 mcg/kg/min; stop Empressin).

On Day 5 the patient was awake, with valid diuresis and reduced noradrenaline (0.04 mcg/kg/min). Indicators of cytolysis were declining (PCT 2.5 ng/ml), although CRP remained high at 19.6 mg/dL, and urine cultures were positive for Escherichia coli and Enterobacter cloacae. Consequently, a third cycle of Cytosorb was initiated. However, it was interrupted due to clotting, leading to a fourth cycle being started.

By Day 6, the patient's condition improved, prompting the initiation of a final cycle of Cytosorb.

Following this treatment, her hemodynamics stabilized without the need for vasopressors, and inflammatory markers normalized (CRP 6.4 mg/dl), supporting her gradual recovery.

A clinical suspicion of zoonosis led to a molecular confirmation revealing Capnocytophaga canimorsus from blood cultures.

Conclusions

The timely diagnosis of septic shock and the therapeutic decision to start antibiotics, corticosteroids and Cytosorb from the onset resulted in a gradual resolution of the multi-organ failure.

A021

Hemoadsorption-Based Strategy For Refractory Chimeric Antigen Receptor T Cell Therapy-Associated Toxicity: A Single Centre Experience

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Introduction

Chimeric antigen receptor T cell (CAR-T) therapy represents a breakthrough in the management of relapsed/refractory hematologic malignancies. Despite its efficacy, it is frequently complicated by cytokine release syndrome (CRS), which can progress to life-threatening organ dysfunction and may not respond to pharmacologic interventions.

Methods

We retrospectively analyzed patients who received CAR-T therapy for hematologic malignancies between 2020 and 2023, focusing on those treated with hemoadsorption. Data collected included demographics, comorbidities, CAR-T details, complications, treatments, and outcomes. Inflammatory markers (IL-6, ferritin, CRP) were measured to assess changes during hemoadsorption. Outcomes included CRS resolution, disease progression, and death. Disease staging, diagnosis and grading of CRS, Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS), acute kidney injury (AKI), and performance status followed established clinical criteria and guidelines.

Results

Among 48 patients, four developed grade 4 CRS unresponsive to standard therapy, including tocilizumab, corticosteroids, and anakinra. These patients—all with high tumor burden and poor performance status—underwent extracorporeal hemoadsorption as additional rescue therapy. Treatment was delivered using continuous veno-venous hemodiafiltration (CVVHDF) with a CytoSorb® cartridge and AN69ST hemofilter.

Hemoadsorption began a mean of 5.2 ± 1.7 days post-CAR-T infusion. One patient, who had refractory IL-6 elevation and pre-existing cardiomyopathy, died shortly after the procedure. The remaining three experienced marked IL-6 reduction (till to –95%), hemodynamic stabilization, improved respiratory function, and renal recovery (Table 1). Two of these patients later succumbed to either disease progression or infection; one survived at least two months after discharge.

Table 1 | Clinical features, CAR-T Therapy, Pharmacological treatment, HA treatments details for each patient

PATIENT	#1	#2	#3	#4
Clinical Features				
Age, years	69	47	77	75
Sex	F	F	M	F
Hematological diagnosis	NOS-DLBCL	NOS-DLBCL	MCL	NOS-DLBCL
Previous therapy lines	2	2	3	2
Disease Stage	4B	4A	3SB	4B

(*Continued*)

(*Continued*)

CAR-T Therapy				
Lymphodepletion regimen	Fluda 25 mg Cy 250 mg	Fluda 25 mg Cy 250 mg	Fluda 30 mg Cy 500 mg	Fluda 25 mg Cy 250 mg
CAR-T product	Tisagenlecleucel	Tisagenlecleucel	Brexucabtagenel	Tisagenlecleucel
Post-infusion complications				
CRS	Yes	Yes	Yes	Yes
-Onset from infusion	0	1	2	1
-Max stage	4	4	4	4
ICANS	Yes	Yes	Not valuable	Yes
-Max stage	4	3	-	4
Other toxicities			Coagulopathy	Cardiomyopathy
Peak IL-6 (ng/L)	>5000 *	4842	4575	2974
Day from infusion	3	3	5	4
Peak CRP (mg/L)	148	221	82	46.6
Peak Ferritin (µg/L)	6564	50565	29330	56401
Peak sCr (mg/dl)	1.9	2.4	1.7	1.5
AKI stage	3	3 (with oliguria)	2	3
Pharmacological treatment				
Tocilizumab	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	1920	1920	1500	1600
Corticosteroids (dexamethasone)	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	170	540	790	270
Anakinra	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	700	1300	700	1400
Blood purification treatment				
Days from CAR-T infusion	7	3	6	5
Modality	CVVHDF	CVVHDF	CVVHDF	CVVHDF
Dialysis Membranes	modified AN69S + *CytoSorb*®	AN69S + *CytoSorb*®	modified AN69S + *CytoSorb*®	AN69S + *CytoSorb*®
HA cycles	2	3	4	1
CVVHDF Duration (days)	6	11	5	1
Delta IL-6 (%)	-95	-88	-67	-18
CRS resolution	Yes	Yes	Yes	No §

Conclusions

This case series highlights the potential role of hemoadsorption as an adjunctive approach for severe CAR-T-related CRS unresponsive to conventional treatment. The therapy was well tolerated and associated with clinical improvement and reduction in inflammatory markers. Nonetheless, further prospective studies with larger cohorts are necessary to validate these findings, refine patient selection, and define optimal integration with existing therapies.

A022

Use Of Cytosorb For Treatment Of CAR-T Therapy-Induced CRS

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Introduction
Chimeric antigen receptor T (CAR-T) cell therapy is a novel treatment for haematological malignancies. Yet, the adverse effects can be severe, like cytokine release syndrome (CRS) and CRS-related coagulopathy.

The typical treatment for CRS involves vital support, Tocilizumab, and hemadsorption to reduce cytokines levels.

Case Report
A 43-year-old patient with IgG lambda multiple myeloma, began Teclistamab treatment in 2023. The day after starting treatment, the patient experienced hyperpyrexia and chest pain, which escalated to cardiogenic shock and cardiac arrest.

After resuscitation, the patient was transferred to the ICU, requiring mechanical ventilation and high doses of catecholamines (noradrenaline 0.8 mcg/kg/min; MAP 60 mmHg; Vasoactive-Inotropic Score VIS 80). Initial blood tests showed high Procalcitonin (PCT) (>100 ng/ml), leukopenia (0.42*10^3/uL), *thrombocytopenia (10**10^3/uL), anemia (HB 8.1 g/dl) and negative culture results. The patient was diagnosed with CAR-T induced CRS and started Tocilizumab therapy.

On day 2, the patient experienced persistent hemodynamic instability (noradrenaline 0.4 mcg/kg/min; MAP 70 mmHg), elevated VIS, PCT > 100 ng/ml, and acute renal failure (Creatinine 2.5 mg/dl). This necessitated the initiation of Continuous Veno-Venous Hemodiafiltration (CVVHDF) and CytoSorb therapy to mitigate the cytokine storm.

During the second CytoSorb cycle, PCT levels significantly decreased to 35.9 ng/ml, hemodynamics and respiratory parameters improved (noradrenaline 0.1 mcg/kg/min; MAP 83 mmHg).

By day 4, after additional CytoSorb administration, inflammatory indices further decreased (PCT 20.4 ng/ml). Noradrenaline administration was discontinued as blood pressure normalized (MAP 87 mmHg), and respiratory weaning began.

On day 5, CVVHDF and CytoSorb treatment were discontinued (Creatinine 0.6 mg/dl), PCT decreased to 8.8 ng/ml, and the patient exhibited stable hemodynamics (MAP 90 mmHg) and valid respiratory exchanges, leading to extubation.

Final hematological assessments on day 6 showed continued reduction in inflammatory markers (PCT 4 ng/ml), improved blood cell count, apyrexia, optimal respiratory exchanges, and normalized blood pressure readings (MAP 97 mmHg). The patient was discharged from the ICU.

Conclusions
In conclusion, the use of CytoSorb helped to mitigate the CAR-T-induced CRS with not side effects or adverse events, and represents a valid supportive treatment for the potentially life-threatening complications of CRS.

A023

Use Of Hemoadsorption In Patients With Septic Shock Of Different Origins: A Case Series

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Introduction
CytoSorb is a certified hemoadsorption device approved for the removal of inflammatory mediators, including both pro- and anti-inflammatory cytokines. Given the

pivotal role of cytokines in mediating macro- and microcirculatory damage in septic shock, its use is supported by a clear therapeutic rationale in this clinical context.

Methods

We report a case series of six patients (median age: 63 years) presenting with septic shock from various causes, including infectious cholecystitis, pneumonia, cardiogenic shock, pulmonary insufficiency, metabolic acidosis, and mediastinitis. All patients exhibited significant respiratory (PaO_2/FiO_2 ratio: 169), hemodynamic (mean arterial pressure: 59 mmHg), and metabolic (lactate: 4.6 mmol/L) disturbances. Due to renal impairment (creatinine: 4.8 mg/dL) and persistent hemodynamic instability, all patients received broad-spectrum antibiotic therapy (e.g., piperacillin/tazobactam, linezolid, fosfomycin, meropenem, fluconazole), continuous renal replacement therapy (CRRT), and three cycles of CytoSorb hemoadsorption (2 CytoSorb in the first day and 1 in the second day) to support organ function and modulate the inflammatory response.

Results

Following a 72-hour CRRT cycle combined with three CytoSorb treatments, patients demonstrated marked improvements in pulmonary, renal, metabolic, and hemodynamic parameters. Lactate levels decreased significantly from 4.55 mmol/L to 1.04 mmol/L, and renal function improved, as indicated by a reduction in serum creatinine from 4.8 mg/dL to 1.1 mg/dL. Oxygenation improved, with PaO_2/FiO_2 increasing from 169 to 321, and mean arterial pressure rose from 59 mmHg to 65 mmHg (figure 1). Overall, four out of six patients were successfully discharged from the intensive care unit, showing clear clinical and laboratory improvement after the combined CRRT and CytoSorb therapy.

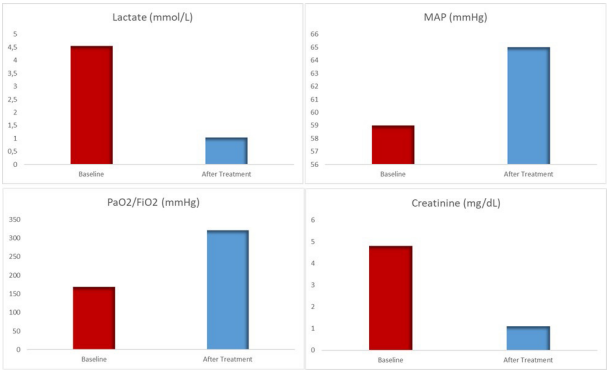

Figure 1 | Lactate, MAP, PaO2/FiO2 ratio, Creatinine, at baseline and after 72 hours of treatment

Conclusion

When added to CRRT in patients with acute renal failure, sorbent therapy demonstrates the ability to improve both hemodynamic stability and overall clinical status in cases of septic shock, regardless of differing epidemiological profiles.

A024

Efficacy Of Cytosorb Use In The Treatment Of Multiple Organ Dysfunction Syndrome Secondary To Salmonella Typhi Sepsis In A 9-Month-Old Paediatric Patient In Intensive Care

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Introduction

Multiple Organ Dysfunction Syndrome (MODS) is a critical condition characterized by decreased functionality of multiple organs secondary to acute infection, which lead to systemic inflammatory response syndrome, sepsis, and septic shock. CytoSorb is a sorbent cartridge made of a polystyrene-divinylbenzene copolymer, certified for modulating the blood concentration of cytokines, which can be a supportive treatment in this sepsis's complication.

Methods
In the case we describe the application of hemadsorption to control MODS induced by Salmonella Typhi Sepsis.

Results
A 9-month-old girl was admitted to the emergency department with hyperpyrexia (Tmax 38.2°C), diarrhea, severe hypotension, oliguria, sinus tachycardia (230 bpm), and SpO2 of 96%. Laboratory tests revealed acute renal failure, liver dysfunction, leukocytosis, and elevated inflammatory markers (CRP 233 mg/L, procalcitonin > 1000 ng/mL).

Due to clinical deterioration, including absence of responses to stimuli, patient required intraosseous hydration, orotracheal intubation, and transfer to Pediatric Intensive Care for MODS management. Broad-spectrum antibiotics (Meropenem, Linezolid, Vancomycin) were initiated alongside adrenaline and noradrenaline for severe hypotension.

Further investigations revealed *Salmonella Typhi* septicemia, along with *Epstein-Barr virus* and *Haemophilus Influenzae* infections.

After failing to respond to antibiotics after four days, CytoSorb therapy combined with Continuous Venovenous Haemodiafiltration (CVVHDF) was started to manage the cytokines storm. Three consecutive sessions (two lasting 12 hours and one lasting 24 hours) led to significant improvement in blood parameters, diuresis, and reduced inflammation (figure 1). Vasopressors and antibiotics were discontinued within 48 hours of CytoSorb initiation.

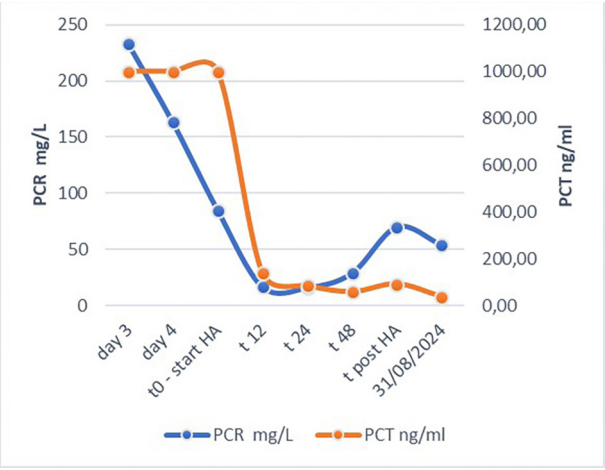

Figure 1 | Inflammation parameters after 3 consecutive CytoSorb sessions

Despite cardiovascular recovery, brain MRI later revealed ischemic cortical damage. After 19 days, she was transferred to Infectious Diseases and Neurology wards with a diagnosis of "tetraparesis secondary to septic shock." She was referred for neurological and nephrological follow-up and rehabilitative therapy.

Conclusions
This case highlights the critical role of advanced intervention with CytoSorb and CVVHDF during the complex MODS management.

A025

CytoSorb Can Support Kidney And Hepatic Function In Severe Septic Shock From Leptospirosis

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Introduction
This study describes a clinical intervention for patients with leptospirosis-related septic shock, specifically focusing on those with acute kidney injury (AKI) and acute liver failure (ALF). The approach combined continuous venovenous hemofiltration (CVVH) with CytoSorb therapy, aiming to reduce the need for vasopressors and improve blood chemistry parameters, such as bilirubin, creatinine, white blood cells (WBC), and C-reactive protein (CRP).

Methods
11 male patients, average age 57 years, were enrolled. All patients had severe AKI (Stage 3) and ALF (MELD Score > 16 or bilirubin > 20 mg/dL). All patients were mechanically ventilated and supported with inotropes. Combined treatment of CVVH and CytoSorb was used: CVVH: 150

ml/min flow rate, dialysis dose at least 40 ml/kg/h (70% pre-dilution). CytoSorb: Cartridge replaced every 24 hours for three consecutive cycles. Anticoagulation: Citrate used in 4 patients.

Results

The starting conditions appeared homogeneous (Saps II 78 ± 6, SOFA 15 ± 5, Apache II 34 ± 6) with high total bilirubin values (>20 mg/dl) and high inflammation indices (WBC, PCR, ESR). There was a significant improvement in vital signs, including reduced vasopressor requirements and improved ventilatory performance. Blood chemistry improved, with a 37.4% reduction in total bilirubin and notable improvements in other markers (creatinine, WBC, PCR). All 11 patients survived, with a prolonged ICU stay (average 31 days).

Conclusion

This combination therapy (CVVH and CytoSorb) was both safe and effective in improving liver and kidney function in patients with leptospirosis-related septic shock, AKI, and ALF. The study suggests that CVVH combined with CytoSorb could be a viable and effective treatment option for critically ill patients with leptospirosis, particularly those with multi-organ failure. The observed reduction in vasopressor doses and improvement in blood chemistry supports the role of this treatment protocol in enhancing organ function and recovery.

A026

Innovative Management Of Malaria-Induced Liver Dysfunction: The Role Of CytoSorb® Hemoadsorption – A Case Report

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Introduction

This case emphasizes the importance of integrating advanced medical technologies with standard therapeutic approaches in the management of severe malaria.

Methods

A 53-year-old man was admitted to our ICU with hyperpyrexia (>38°C), dyspnea, asthenia, mental confusion, anemia, and hyperbilirubinemia after recent travel to Africa. PCR diagnostic testing confirmed Plasmodium falciparum malaria with 30% parasitemia. Blood tests showed elevated PCT (>100 ng/ml), CRP (20 mg/dL), Hb (8.0 g/dL), total bilirubin (32 mg/dL, direct bilirubin 20 mg/dL), pancreatic amylase 241 IU/L, lipase 253 IU/L, creatinine 1.6 mg/dL Imaging via CT scan revealed moderate bilateral pleural and perihepatic effusion. Despite these findings, hemodynamic and respiratory parameters remained stable, with high-flow oxygentherapy proving sufficient. Diuresis was always maintained. Intravenous artesunate was administered at 240 mg (T0, T12, T24, T48), under QT interval monitoring, accompanied by supportive therapy. To address persistently high bilirubin and inflammation markers, extracorporeal hemoperfusion adsorption (E.H.A.) with a CytoSorb® filter started on the third day for 24 hours under continuous heparin infusion.

Results

The procedure yielded significant laboratory improvements, notably in bilirubin and PCT/CRP reduction, Fig.1, while anemia was managed through transfusion. A second E.H.A. cycle was implemented on the fourth day, resulting in further clinical and laboratory enhancements. On the fifth day, the patient commenced a three-day antimalarial course of Atovaquone/Proguanil (250 mg/100 mg/day).

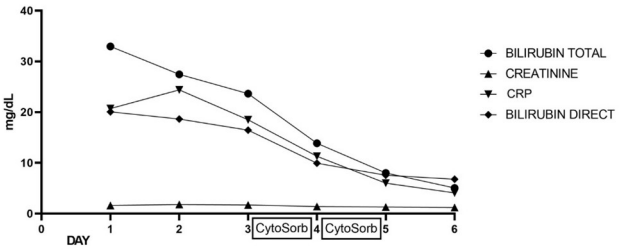

Figure 1 | Bilirubin, Creatinine and CRP trend

By the eighth day, he was stable enough to be transferred to the infectious diseases ward and was eventually discharged home on the fourteenth day.

Conclusion

E.H.A. with CytoSorb® disrupted the albumin-bilirubin complex and effectively adsorbed bilirubin, addressing hyperbilirubinemia and cytokine overload. This intervention served as a crucial "bridge" therapy, enabling the antimalarial regimen to take effect. The patient's rapid improvement, evidenced by reduced bilirubin levels, enhanced neurological status, and resolution of jaundice, highlights the potential of E.H.A. as an adjunct treatment in complex malaria cases.

A027

Sepsis And Cytokine Storm: The Role of Dialytic Techniques In The Different Stages Of A Rapidly Progressive Disease

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Introduction

Despite advancements in research and numerous clinical studies on innovative therapies, no new pharmacological agent has been proven to significantly improve survival in septic shock. Understanding the role of pro-inflammatory cytokines in disease progression, particularly in the transition from reversibility to irreversibility, has led to the development of extracorporeal therapies capable of altering the course of this rapidly worsening condition.

The irreversibility of septic shock is primarily determined by microcirculatory dysfunction and vasoplegia that is resistant to fluid resuscitation and vasoactive drugs. The continuous removal of cyclically produced pro- and anti-inflammatory mediators contributes to immune modulation and the restoration of the patient's immune homeostasis. Acute kidney injury (AKI) complicates 19% of sepsis cases, 23% of severe sepsis cases, and 50% of septic shock cases, with an unfavorable prognosis in 75% of patients.

Methods

A meta-analysis conducted by Kellum et al. (2013) demonstrated that extracorporeal purification therapies can reduce mortality in septic patients. Techniques such as hemoperfusion, plasma filtration, and hemoadsorption have significantly improved hemodynamics and organ function. Hemoperfusion with Toraymyxin®, used in shock caused by Gram-negative bacteria, selectively removes over 90% of circulating lipopolysaccharide in two 120-minute sessions, 24 hours apart. Clinical studies have confirmed its efficacy in patients refractory to conventional medical therapy.

Results

Plasma filtration (CPFA®) and hemoadsorption (Cytosorb®, Oxiris®) have proven effective in reducing mortality in patients who have progressed to the irreversible stage. The success of the therapy is closely related to the timing of initiation and the patient's early hemodynamic response. A retrospective study by Votrico et al. (2020-2022) on 59 patients with S-AKI treated with CRRT and Cytosorb showed that more intensive treatment (duration $\geq$ 72h) resulted in better hemodynamic stability (SBP, DBP, MAP) and improved inflammatory marker trends (CRP, PCT).

Conclusions

Available evidence supports the efficacy of extracorporeal purification techniques in improving survival in critically ill patients. Multidisciplinary collaboration between intensivists and nephrologists remains crucial to optimizing treatment timing and potentially developing shared guidelines for managing this otherwise challenging condition.

Reference

Zhou F, Peng Z, Murugan R, Kellum JA. Blood purification and mortality in sepsis: a meta-analysis of randomized trials. Crit Care Med. 2013 Sep;41(9):2209-20. doi: 10.1097/CCM.0b013e31828cf412. PMID:23860248; PMCID: PMC3758418.

A028

Septic Shock And IL-6: Impact Of Cytosorb® Therapy In A High-Complexity Case

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Introduction

Interleukin-6 (IL-6) is a key cytokine involved in the regulation of inflammation and immune response. Its overproduction has been implicated in various pathological conditions, including sepsis, autoimmune diseases, and hyperinflammatory syndromes.

Early adoption of extracorporeal support therapies such as Continuous Renal Replacement Therapy (CRRT) combined with **Cytosorb®**—the only certified adsorber cartridge for whole blood removal of cytokines, bilirubin, myoglobin, Ticagrelor, and Rivaroxaban—can lead to significant clinical improvement by counteracting the progression toward septic shock and improving outcomes in critically ill patients.

Methods

A 71-year-old male on thrice-weekly hemodialysis presented with multiple comorbidities, including obesity, rheumatoid arthritis, hypertension, type 2 diabetes mellitus, and a history of COVID-19 pneumonia. He was admitted to the ICU for severe CVC-related sepsis and underwent Continuous Renal Replacement Therapy (CRRT) in CVVHDF modality with **Cytosorb®** for 48 hours from the diagnosis of septic shock.

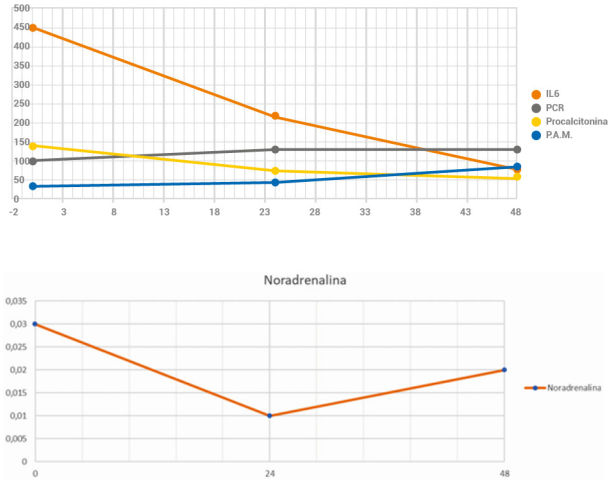

Figure 1 | 1a and 1b: Hemodynamic stabilization and attenuation of the systemic inflammatory response, reflected by a decrease of the parameters

The following parameters were monitored during treatment:

- Plasma IL-6 levels
- Inflammatory markers (CRP)
- Vital signs and vasopressor support requirements
- Progressive reduction in norepinephrine dosage

Results

Within the first 24 hours, a marked clinical improvement was observed, including stabilization of vital signs, adequate blood pressure control, and reduced need for vasopressor support. Inflammatory markers decreased rapidly, and IL-6 plasma levels dropped from 452 pg/mL at the start of therapy to 78 pg/mL at the end of treatment with **Cytosorb®** (see Figure 1a and 1b).

Conclusion

The use of **Cytosorb®** played a pivotal role in the rapid resolution of septic shock, contributing to both hemodynamic stabilization and attenuation of the systemic inflammatory response. This clinical case supports the rationale for early implementation of hemoadsorption techniques in critically ill patients, highlighting the potential benefits of prompt intervention for rapid clinical and inflammatory improvement.

A029

Effects Of Continuous Veno-Venous Hemodiafiltration On Biomarkers And Outcomes In Acute Liver Injury Induced By Abdominal Sepsis Using CytoSorb®: A Case Report

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Introduction

Acute hepatocolangitis is an infection of the biliary tract that can rapidly progress to abdominal sepsis and subsequent acute liver injury if not promptly treated. The standard management involves broad-spectrum antibiotics, supportive medical therapy, and surgical intervention when needed. However, in cases of septic shock, conventional treatment may not be sufficient. CytoSorb® hemoadsorption therapy has been developed to remove excessive cytokines and other inflammatory mediators from the bloodstream, aiming to modulate the hyperinflammatory state and stabilize hemodynamics[1;2;3]

Methods

We report the case of a 56-year-old Caucasian woman, admitted for surgical revision due to anastomotic stenosis. Postoperatively, she developed acute hepatocolangitis. Upon ICU admission, she presented a qSOFA score of 2 and lactates at 9.3 mmol/L. Despite broad-spectrum antibiotics and vasopressor support, her condition deteriorated with a progressive rise in lactate levels (14.5 mmol/L). Continuous Veno-Venous hemodiafiltration (CVVHD) was initiated, resulting in a modest lactate reduction (12 mmol/L). Due to persistent Hyperbilirubinemia and abnormal liver function parameters, CytoSorb® was integrated into the extracorporeal circuit. At the time of CytoSorb® initiation, lactate was measured at 9.8 mmol/L.

Results

Following the combination of CytoSorb®, a rapid decrease in lactate levels was observed: 1.9 mmol/L within three hours (figure 1). Hemodynamic stabilization enabled the cessation of norepinephrine infusion. Renal function improved with spontaneous diuresis recovery, while hepatic and inflammatory markers normalized. By the third day, CVVHD was discontinued, and the patient was transferred back to the surgical unit in stable condition.

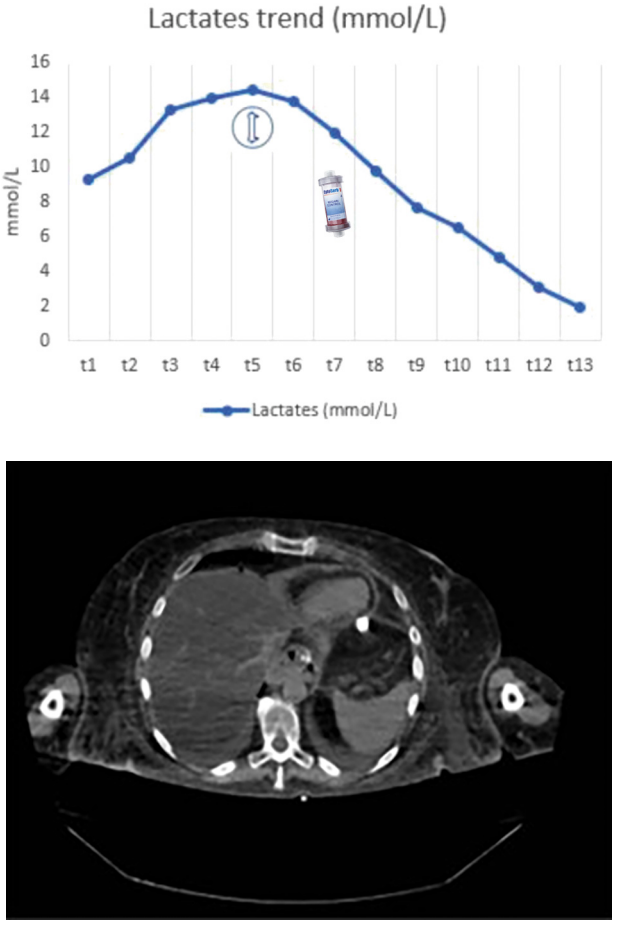

Figure 1 | Lactates trend and diagnostic imaging

Conclusions

This case highlights the critical role of extracorporeal blood purification in septic patient resuscitation. The early integration of CytoSorb® into standard CVVHD significantly enhanced lactate clearance and inflammatory biomarker reduction, promoting rapid clinical stabilization. Our findings suggest that hemoadsorption may serve as a valuable adjunctive therapy in abdominal sepsis complicated by acute liver dysfunction, with potential benefits in improving clinical outcomes.

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A030

CytoSorb® Hemoadsorption In Septic Shock After Colorectal Surgery: A Case Report

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Background

Sepsis is a life-threatening condition caused by a dysregulated host response to infection, which can evolve into septic shock, marked by severe circulatory abnormalities requiring vasopressor support. CytoSorb® is an extracorporeal hemoadsorption therapy designed to modulate inflammatory mediators in the bloodstream, to aid hemodynamic stabilization. We present a case of postoperative septic shock treated with CytoSorb® following colorectal surgery.

Methods

A 74-year-old man with a previous rectal resection, underwent a colorectal anastomosis to close the ileostomy. Three days after surgery, he began to show progressive clinical deterioration. CT imaging revealed mesenteric fat stranding and a fluid collection in the right iliac fossa. After one week, he was admitted to the intensive care unit in septic shock, with elevated lactate levels and requiring vasopressor support (norepinephrine at 0.12 mcg/kg/min and vasopressin at 2.4 U/h). He underwent emergency surgery for new stoma creation. Upon return to the ICU, vasopressor requirements had increased (norepinephrine at 0.35 mcg/kg/min, adrenaline at 0.1 mcg/kg/min, and vasopressin at 4 U/h). Thus, led to start CytoSorb® therapy, continued for a total of three cartridges.

Results

Over the course of CytoSorb® treatment, a progressive reduction in vasopressor doses was observed. Norepinephrine dropped to 0.1 mcg/kg/min by the end of the third cartridge. Adrenaline was reduced from 0.1 to 0.06 mcg/kg/min, while vasopressin, was completely discontinued by Day 3. In parallel, the white blood cell count increased to 3.3 $\times 10^3/\mu L$, reflecting a recovery from initial immunosuppression. The patient showed progressive clinical improvement and was successfully extubated one week after starting CytoSorb® (Figure 1).

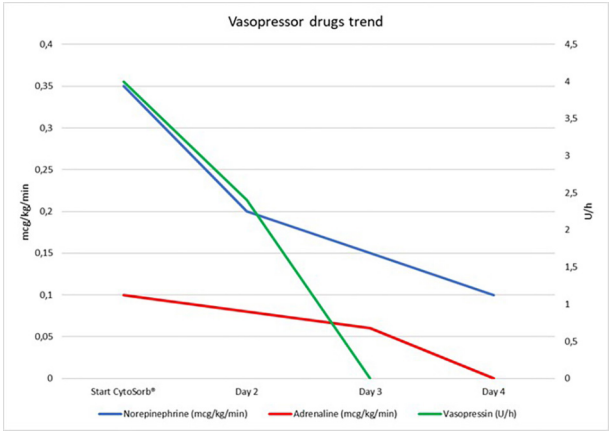

Figure 1 | Vasopressor drugs trend during CytoSorb® treatment

Conclusion

This case illustrates how CytoSorb® therapy may help in the management of septic shock following major abdominal surgery. The treatment was associated with a marked reduction in vasopressor requirements and clinical stabilization, supporting its potential role in improving outcomes in severe postoperative sepsis.

A031

Impact Of Hemoadsorption With CytoSorb® In A Case Of Streptococcus Pneumoniae-Induced Septic Shock

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Introduction

Sepsis is a severe systemic inflammatory response to infection that can rapidly progress to septic shock and multiorgan failure.

Timely initiation of extracorporeal support therapies such as continuous renal replacement therapy (CRRT) combined with CytoSorb® -the only adsorber cartridge certified for whole blood removal of cytokines, bilirubin, myoglobin, ticagrelor, and rivaroxaban- can significantly improve clinical parameters by counteracting the progression to septic shock and improving outcomes in critically ill patients.

Methods

A 42-year-old asplenic woman presented to the emergency department with vomiting, diarrhea, fever, facial erythema with cyanosis, petechiae on the trunk and lower limbs, and signs of peripheral hypoperfusion. She tested positive for Streptococcus pneumoniae urinary antigen and was promptly started on antibiotic therapy. During hospitalization, she required a surgical tracheostomy and subsequently developed critical ischemia of both upper and lower extremities, necessitating multiple amputations.

She underwent continuous veno-venous hemodialysis (CVVHD) using an EMiC filter in combination with CytoSorb® to treat a cytokine storm and improve hemodynamic stability.

Early initiation of CVVHD with an EMiC filter and CytoSorb® therapy was thus chosen, aiming to mitigate the cytokine storm responsible for organ dysfunction and to improve the patient's hemodynamic profile.

Results

Vital signs stabilized, blood pressure was well controlled, and vasopressor requirements decreased. Procalcitonin (PCT) levels dropped from 31.8 µg/L to 14 µg/L and serum creatinine decreased from 2.34 mg/dL to 1.46 mg/dL by day three, with a continued downward trend toward normalization. Systolic blood remained stable and subsequently increased (Figure 1).

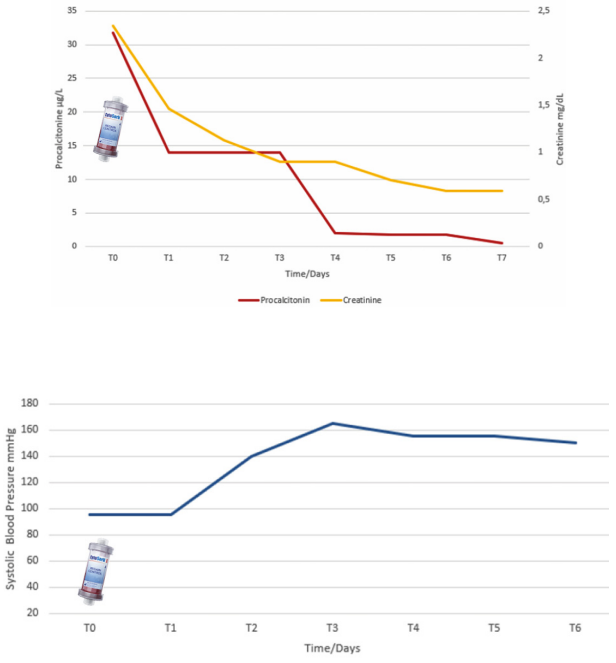

Figure 1 | PCT, Creatinine and SBP levels after CytoSorb treatment

Conclusion
CytoSorb® therapy played a key role in the rapid resolution of septic shock, contributing to both hemodynamic stabilization and attenuation of the systemic inflammatory response.

This clinical case supports the rationale for early use of hemoadsorption techniques in critically ill patients, highlighting the potential benefits of timely intervention to achieve rapid clinical and inflammatory improvement.

A032

Extracorporeal Hemoadsorption In A Patient With Septic Shock: Our Experience

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Introduction
Septic shock is a severe syndrome with high mortality, characterized by significant multi-organ dysfunction and early acute kidney failure. This condition is caused by an excessive and dysregulated inflammatory response of the body to infectious agents, primarily bacteria.

Methods
65-year-old female, depressive syndrome, no allergies.

Sepsis due to urinary lithiasis, progressed to septic shock. In Intensive Care Unit started intensive therapy with effective respiratory exchange and hemodynamics supported by amines (norepinephrine 0.9 mcg/kg/min) and vasopressin (0.03 IU/ml). Early initiation of CRRT (Continuous Renal Replacement Therapy) and extracorporeal hemoadsorption using Alteco and Cytosorb filters:

- CVVHD with citrate for 144 hours (72 h + 72 h) + extracorporeal hemoadsorption with 1 Alteco filter for 6 hours and 1 Cytosorb filter for 9 hours + an additional Cytosorb filter for 15 hours
  - Qb: 125 ± 32 ml/min, Qd: 2033 ± 201 ml/h, U.F.: 0
  - Citrate dose: 3.2 ± 0.4 mmol/l, Calcium dose: 1.9 ± 0.3 mmol/l
- CVVHDF with citrate for 140 hours (72 h + 68 h)
  - Qb: 128 ± 40 ml/min, Qd: 2766 ± 100 ml/h, infusion: 1511 ± 30 ml/h, U.F.: 0
  - Citrate dose: 4.7 ± 0.2 mmol/l, Calcium dose: 1.6 ± 0.1 mmol/l

Results
On admission to ICU (see Table 1): Blood pressure: 70/44 mmHg, Mean arterial pressure: 55 mmHg,

Heart rate: 110 bpm. SAPS-II: 40, SOFA score: 15
Oligo-anuria with acute kidney injury.

At discharge (see Table 1): Blood pressure: 154/71 mmHg, Mean arterial pressure: 101 mmHg

Heart rate: 80 bpm
Diuresis and GFR preserved

Conclusions
The early use of CRRT with high cut-off filters and extracorporeal hemoadsorption with filters specific for lipo-

Table 1 | Parameters ICU admission and discharge

	Creat mg/dl	GFR ml/min	K mmol/l	Hb g/dl	PLT	PCR mg/l	ATIII %	procalcitonina ng/mL	lattati mmol/L	HCO3 mmol/l
T.I. (IN)	2.5	20	3.4	11.5	80.000	32.3	60	216	17	12.6
T.I. (OUT)	0.8	90	3.9	13.7	300.000	12.6	100	0.16	1.6	25.9

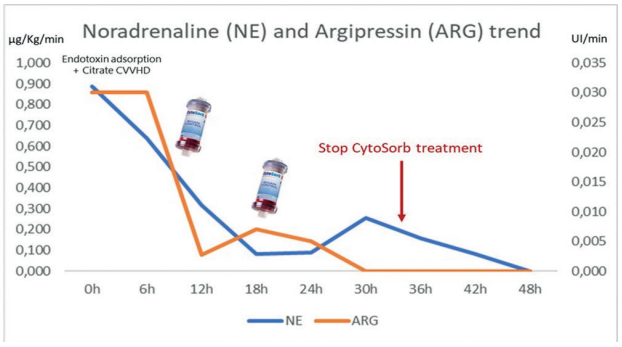

Figure 1 | Noradrenaline and Argipressin trend

proteins and pro- and anti- inflammatory cytokines improves the prognosis and outcome of patients in septic shock, allowing for greater and faster modulation of the cytokine cascade, better restoration of homeostasis and hemodynamic stability, early discontinuation of vasopressors (fig.1), and preservation of renal function and diuresis.

A033

Intestinal Perforation Complicated By Necrotizing Fasciitis Resulting In Septic Shock From Clostridium Septicum Treated With CytoSorb

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Introduction

Febrile neutropenia (FN) is a potentially life-threatening complication of systemic chemotherapy. Prompt diagnosis is critical, as delays in initiating antimicrobial therapy are linked to poorer outcomes. Clostridium septicum bacteremia is a rare cause of FN, with only a few cases reported in the literature,

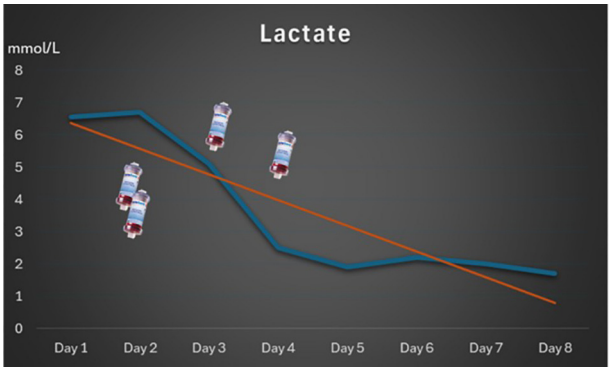
Methods

We report the case of a patient who presented with cecal and ascending colon perforation, associated with marked and diffuse edematous-inflammatory thickening of the bowel walls involving the cecum, ascending colon, and proximal transverse colon. Given the CT findings, recent chemotherapy administration, and laboratory evidence of severe leukopenia (WBC 1.2 × 10^9/L) with neutropenia, a diagnosis of neutropenic enterocolitis complicated by intestinal perforation was strongly suspected. The patient underwent an exploratory laparotomy with a right hemicolectomy. Postoperatively, the patient was admitted to the intensive care unit in septic shock, requiring high-dose vasopressor support. Continuous renal replacement therapy (CRRT) with continuous veno-venous hemodialysis (CVVHD) was initiated on day 2, using also CytoSorb. A total of 4 CytoSorb cartridges were used: the first two were replaced every 12 hours, and the subsequent two every 24 hours. In addition, the patient received a three-day course of IgM-enriched intravenous immunoglobulins.

As a complication of septic shock caused by *Clostridium septicum*, the patient developed necrotizing gluteal-lumbar fasciitis, which required multiple fasciotomies and hyperbaric oxygen therapy.

Results

Following CRRT combined with CytoSorb, the patient's hemodynamic status showed improvement (Fig.1). Renal function gradually recovered. Over time, renal function fully normalized, and after a prolonged rehabilitation period, the patient was discharged.



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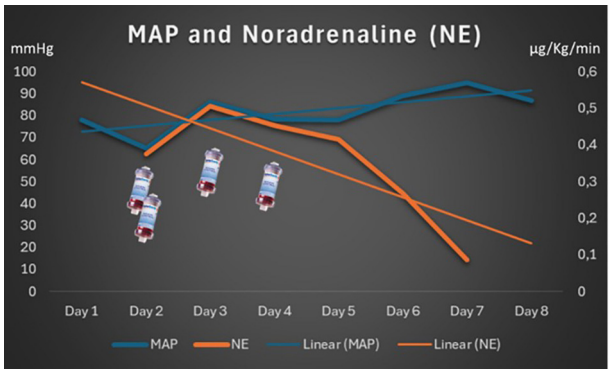

Figure 1 | Lactate, MAP and Noradrenaline levels during treatment period

Conclusion

This case highlights the importance of early recognition and aggressive management of neutropenic enterocolitis, and Clostridium Septicum gas gangrene, a life-threatening complication in patients undergoing chemotherapy. The use of advanced therapies, including CRRT with CytoSorb and IgM-enriched immunoglobulins, may contribute to stabilization in cases of septic shock.

A034

CytoSorb® Hemoadsorption Therapy Effects On Myoglobin And Renal Function In Rhabdomyolysis: A Case Series

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Introduction

Rhabdomyolysis is a condition characterized by skeletal muscle breakdown and the release of myoglobin and creatine kinase (CPK). The resulting renal overload can lead to acute kidney injury (AKI). Cytosorb is an extracorporeal adsorption cartridge certified for rapid myoglobin removal. This study analyses the use of Cytosorb in patients with severe rhabdomyolysis.

Methods

This retrospective analysis includes data from intensive care unit (ICU) patients with rhabdomyolysis treated with continuous renal replacement therapy combined with Cytosorb cartridge. Patient demographics, etiology of rhabdomyolysis, presence and severity of AKI were registered. The study examined myoglobin and CPK levels at admission and during treatment. Duration of treatment and the number of cartridges used per patient were reported. Additionally, correlations between Cytosorb use and renal function improvement were explored.

Results

Patients' median age was 58 years. 80% of rhabdomyolysis was caused by crush syndrome. At admission median AKI stage was 1. At treatment initiation median values of myoglobin and CPK were 18455 ng/ml and 12126 , respectively (see Fig.1). Cytosorb therapy was initiated within a median of 24 hours from ICU admission. The median treatment duration was 24 hours, with a median of 1 cartridge used per patient. At the end of the treatment a significant decrease in myoglobin and CPK levels was observed (median 418 ng/ml, p=0.007 and 1396 U/L, p=0.039, respectively). In 60% of cases AKI was resolved at discharge, in the remaining AKI stage improved; also, the cumulative daily dose of furosemide reduced significantly (median 120 mg/die *vs* 20 mg/die, p=0.04).

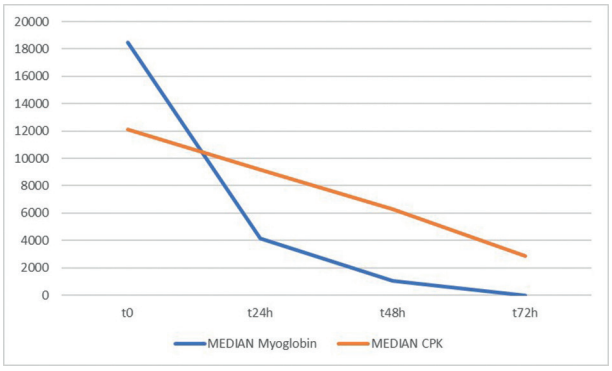

Figure 1 | Median myoglobin and CPK trend during treatment

Conclusions

The use of Cytosorb in patients with rhabdomyolysis showed potential benefits in reducing myoglobin and CPK levels, with an improvement in renal function. Early treatment initiation and the number of cartridges used appeared to positively influence clinical outcomes. Further studies are needed to confirm efficacy and establish optimal treatment protocols.

A035

Blood Purification Techniques In Septic Patients: A Comparison Between Two Different Strategies

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Introduction

Septic patients can be effectively treated using various blood purification techniques. Such therapies support organ function and improve outcomes by controlling the systemic inflammatory response often seen in severe sepsis and septic shock..

Methods

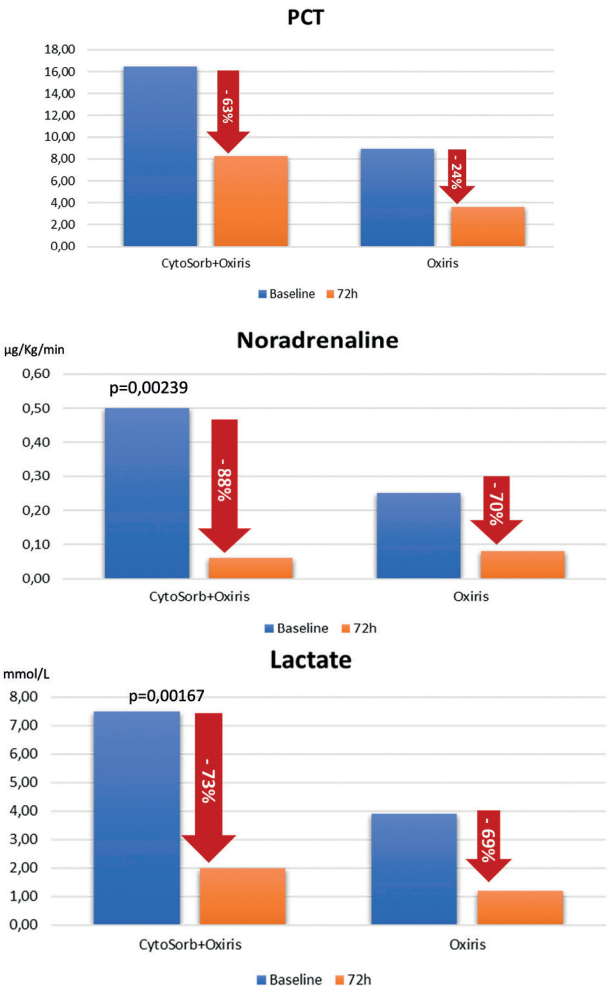
We present a case series of 18 septic patients with stage 3 acute kidney injury (AKI), treated using continuous renal replacement therapy (CRRT). Five patients received CRRT with Oxiris alone, while thirteen received CRRT with Oxiris plus CytoSorb. Treatment was personalized based on each patient's clinical profile and progression. Patients in the CytoSorb group were more severely ill.

Results

CytoSorb group has shown a stronger tendency than Oxiris group in improving several parameters at 72h, such as creatinine reduction (from 2,41 mg/dl to 0,61 mg/dl, reduction: 75% and from 2,35 mg/dl to 1,40 mg/dl, reduction: 41% respectively); PCR reduction (from 31,18 mg/dl to 16,45 mg/dl, reduction: 47% and from 12,02 mg/dl to 8,94 mg/dl, reduction: 26% respectively); PCT reduction (from 16,45 ng/ml to 8,25 ng/ml, reduction: 63% and from 8,94 ng/ml to 3,64 ng/ml, reduction: 24% respectively); Noradrenaline reduction (from 0,5 micg/Kg/min to 0,06 micg/Kg/min, reduction: 88% and from 0,25 micg/Kg/min to 0,08 micg/Kg/min, reduction: 70% respectively); lactate reduction (from 7,5 mmol/l to 2 mmol/l, reduction: 73% and from 3,9 mmol/l to 1,2 mmol/l, reduction: 69%); Length Of Stay reduction (12 days and 18 days in CytoSorb group and Oxiris group respectively); SOFA reduction (from 14 to 7, reduction: 50% and from 18 to 10, reduction: 44% respectively); rate of kidney function recovery (63% in CytoSorb group and 40% in Oxiris group, respectively).

Conclusion

Our experience suggests that these therapies may contribute to improvements in metabolic parameters,



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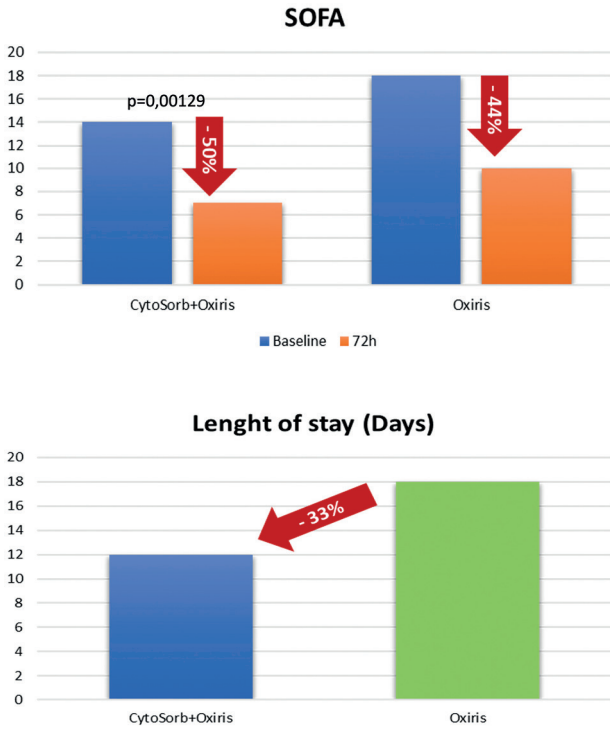

Figure 1 | Values of PCT, Noradrenaline, Lactate, SOFA and LOS from baseline to 72h

hemodynamic status, kidney function, SOFA scores and length of stay reduction in intensive care. Comparative data indicate that combining CytoSorb with Oxiris offers synergistic benefits over Oxiris alone (Figure 1).

A036

CytoSorb In Septic Shock With Multiorgan Failure Secondary To Methicillin-Sensitive Staphylococcus Aureus (MSSA): A Case Report

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Introduction

A 49-year-old male with a history of intravenous drug use was admitted to the ICU in a state of profound septic shock and multiorgan failure (MOF), secondary to methicillin-sensitive *Staphylococcus aureus* (MSSA) pneumonia and acute polysubstance intoxication. On arrival, he was hypotensive and tachycardic, requiring high-dose vasopressors. Initial labs revealed severe acute kidney injury (creatinine 10.57 mg/dL), coagulopathy (platelets 122,000/mmc, INR 1.3) and an extremely elevated procalcitonin (PCT 454.70 ng/mL), indicative of a hyperinflammatory cytokine storm. A diagnosis of pneumonia with parenchymal consolidations was confirmed radiologically. Given the clinical severity, early initiation of CytoSorb hemoadsorption therapy was undertaken as adjunct to supportive care.

Methods

Continuous veno-venous hemodiafiltration (CVVHDF) was started approximately 6 hours post-ICU admission, in conjunction with a single CytoSorb cartridge which was used continuously for 23 hours. Hemodynamic assessment was conducted using the MostCare monitoring system which provided real-time advanced metrics including cardiac index (CI), systemic vascular resistance index (SVRI), and dP/dt MAX. Dobutamine was added 6 hours after CytoSorb commencement due to persistent hemodynamic instability despite optimized volume resuscitation and dual vasopressor therapy.

Results

Following initiation of CytoSorb, progressive hemodynamic improvement was noted. Argipressin was discontinued at 16 hours, Norepinephrine at 42 hours, and Dobutamine at 66 hours. A decrease in CI from 4.0 to 2.7 L/min/m^2 and an increase in SVRI from 1500 to 2300 dyn·s·cm^{-5}·m^2 reflected recovery of vascular tone and attenuation of hyperdynamic circulation. Contractility, as measured by dP/dt MAX, improved from 0.8 to 1.2 mmHg/ms. Renal function significantly improved (creatinine dropped to 3.0 mg/dL), PCT fell notably and the patient was successfully extubated on day 15 and transferred to the medical ward on day 21.

Conclusion

This case highlights the potential benefit of early CytoSorb use in combination with CVVHDF and MostCare-guided hemodynamic management in patients with refractory septic shock. The rapid weaning from vasopressors, along

with favorable trends in CI, SVRI, and dP/dt MAX, supports the hypothesis that targeted cytokine removal can modulate the dysregulated host response in sepsis. This aligns with emerging evidence suggesting improved short-term survival and hemodynamic stabilization with CytoSorb therapy.

A037

The Golden Hour In The Timely Therapeutic Treatment With CVVHD And CytoSorb In A Patient With Severe Septic Shock

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Introduction

The "golden hour" in sepsis treatment is critical; early recognition and intervention significantly improve survival. Administering antibiotics, fluids, and source control within this window reduces organ failure and mortality. Prompt care during this first hour is essential for optimal outcomes in septic patients, also with extracorporeal therapies for blood purification as CRRT and hemoadsorption.

Methods

A 52-year-old patient presented to the emergency room with a high fever, redness, swelling, and pain in his right arm, suggestive of an infectious condition—possibly erysipelas—potentially caused by an insect bite or injury from a contaminated object. Due to worsening clinical status and vital signs, along with the onset of septic shock and acute renal failure, he was admitted to the intensive care unit. Hemodynamic support was initiated with norepinephrine due to severe hypotension secondary to septic shock. From the first day of hospitalization, the patient underwent hemofiltration using a CVVHD machine in combination with CytoSorb therapy. Three sessions of CVVHD were performed, each with a new CytoSorb cartridge.

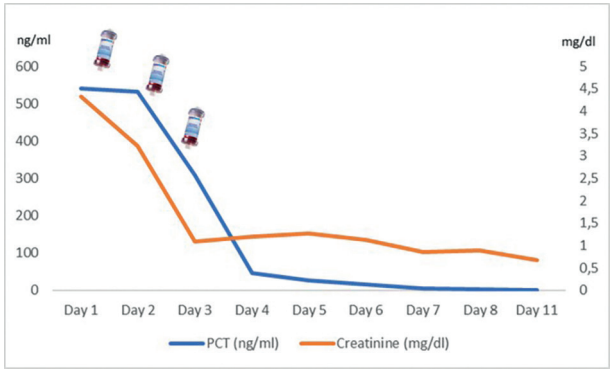

Figure 1 | PCT and Creatinine trend

Results

On day 3, CytoSorb and CRRT treatments were discontinued, as the infection and sepsis had fully resolved. The patient showed improved vital signs, regained full hemodynamic stability (with norepinephrine gradually tapered and permanently stopped by day 3), and experienced recovery of both renal and respiratory function. Laboratory markers, including procalcitonin and creatinine (see Figure 1), showed consistent improvement. Broad-spectrum empiric antibiotic therapy was continued despite negative culture results. The antibiotics administered included meropenem, daptomycin, clindamycin, and doxycycline.

Conclusion

This case highlights the importance of early recognition and aggressive management of sepsis and septic shock. The combination of timely antibiotic therapy, hemodynamic support, and advanced blood purification strategies—specifically CVVHD and CytoSorb therapy—played a crucial role in the rapid clinical improvement and organ function recovery of the patient.

A038

Purification Treatment With Cytosorb® As A Bridge To Emapalumab In A Severe Case Of Macrophage Activation Syndrome Secondary To Systemic Lupus erythematosus

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Introduction

We report the case of a young girl with a past medical history of vertically transmitted C hepatitis, treated with ledipasvir/sofosbuvir at the age of 12, obtaining a persistent negativization of viraemia.

Methods

At 14 years of age, she was diagnosed with systemic lupus erythematosus with class IV-V lupus nephritis determining anuric AKI that required hemodialysis for 3 weeks. She received hydroxychloroquine, high dose steroids, i.v. cyclophosphamide, plasma-exchange and showed good recovery of renal function.

She developed thrombotic microangiopathy and was therefore started on eculizumab, showing a good clinical response.

Three months after the disease onset, while she was on maintenance therapy with prednisone, hydroxychloroquine and eculizumab, she was re-hospitalized for severe fluid overload and diagnosed with macrophage activation syndrome. She showed very poor response to standard treatment with high dose steroids and anakinra; as a rescue therapy emapalumab was therefore requested, but was not immediately available.

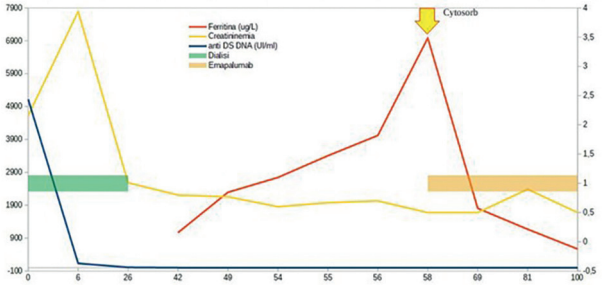

Figure 1 | Ferritin trend before and after CytoSorb treatment

Results

Considering the very severe clinical presentation (anasarca in pseudo pseudo Meigs syndrome secondary to SLE, lymphopenia, hypofibrinogenemia, hyperferritinemia) with still impaired renal function, a double-lumen CVC was placed and an extracorporeal blood purification treatment with Cytosorb was carried on for 24 hours with a stand-alone application on a Prismax RRT machine; hemodynamics remained stable and no side effects were observed. The patient was then started on emapalumab, showing a good clinical response with complete resolution of macrophage activation syndrome within 6 weeks (see Fig.1).

Conclusion

After 8 months period of follow up she is showing no disease activity with normal ferritine, negative anti DS DNA antibodies and normal glomerular filtration rate (110 ml/min/1.73mq).

A039

Use Of The CytoSorb® In Septic Shock: A Narrative Review

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Introduction
Septic shock represents a critical clinical condition characterized by a disproportionate systemic inflammatory response to infection, often complicated by multiorgan failure (MOF) and high mortality rates. CytoSorb is an adjunctive therapeutic support capable of adsorbing cytokines, bilirubin, myoglobin, toxins, and drugs, thereby improving patient clinical outcomes. This narrative review presents six cases of critically ill patients with septic shock treated with CytoSorb in combination with Continuous Renal Replacement Therapies (CRRT), highlighting the positive clinical effects observed.

Methods
Six clinical cases were selected, all characterized by refractory septic shock complicated by multiorgan failure. Patients had APACHE IV scores ranging from 60 to 100, corresponding to estimated mortality rates between 40% and over 90%. All patients were treated with CytoSorb integrated into CRRT, with treatment duration ranging from 12 to 72 hours (average duration: 60 hours).

Results
All cases showed recovery of urine output, improvement in renal function indices, and normalization of lactate levels, with discontinuation of vasopressor support within 72 hours from treatment initiation. In five patients, hepatic and/or respiratory dysfunction resolved as well, allowing for extubation or decannulation. In two cases of CMV (Cytomegalovirus) and EBV (Epstein-Barr Virus) infection, and drug overdose, the treatment contributed to the removal of toxic and immunologic agents. All patients survived the critical phase and were transferred to non-intensive care units. No adverse events related to CytoSorb therapy were reported.

Conclusion
Hemoadsorption therapy with CytoSorb, combined with CRRT, demonstrated a favorable impact on early stabilization of patients with septic shock and MOF, even in complex clinical scenarios with poor prognostic scores. Although based on a limited case series, these findings suggest a potential role for CytoSorb in attenuating the cytokine storm and promoting organ function recovery.

CytoSorb confirms as an effective and potentially life-saving adjunctive therapy, significantly improving outcomes in critically ill patients by reducing the need for intensive support and accelerating clinical stabilization.

A040

One-Year Single-Center Experience Of Extracorporeal Blood Purification Therapies In Critically Ill Patients: Selection Criteria, Timing And Predictors Of Outcome

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Introduction
Septic shock is one of the leading causes of mortality in critically ill patients and is often associated with multiorgan dysfunction. Extracorporeal blood purification therapies (EBPT), such as Continuous Renal Replacement Therapy (CRRT) combined with CytoSorb®, enable the removal of cytokines, bilirubin, myoglobin, and toxins, with potential clinical benefits.

This single-center study describes the use of CytoSorb® in critically ill patients with septic shock (predominantly), acute liver failure, rhabdomyolysis, and various intoxications, analyzing timing of initiation, patient selection criteria, and clinical impact, with the aim of optimizing EBPT use in intensive care.

Methods
A retrospective analysis was conducted on 38 patients treated in 2024 with hemoadsorption using CytoSorb® combined with CRRT. In patients with septic shock, inclusion criteria were AKI stage KDIGO 2–3, norepinephrine requirement >0.5 mcg/kg/min, lactate >2 mmol/L, and SOFA score >8, with therapy initiated within 48 hours from the start of resuscitation.

In cases of rhabdomyolysis, acute liver failure, or intoxications, treatment was started early after diagnosis. In selected cases, oXiris® filters were also used.

Results

Patients' distribution was as follows: 31 with septic shock, 3 with acute liver failure, 2 with rhabdomyolysis, and 2 with intoxications. Overall mortality was 43%, mainly among septic patients with inadequate or delayed source control. Survivors were generally younger (58 vs. 70 years) and had significantly lower SAPS II and CCI scores.

In survivors, treatment was initiated earlier (13.7 h vs. 18 h, $p<0.05$), with shorter vasopressor duration and lower lactate levels. No deaths occurred among patients with rhabdomyolysis or acute liver failure.

Conclusion

Hemoadsorption with CytoSorb® appears to be a promising therapeutic option in critically ill patients, especially when initiated early in the course of multiorgan dysfunction. The benefit is more evident in clinical contexts with high toxic burden, such as rhabdomyolysis, acute liver failure, or severe intoxications. In septic shock, timely infection source control remains essential, but extracorporeal support may facilitate hemodynamic stabilization and reversal of shock.

A041

Use Of Cytosorb Cartridges In A Case Of Systemic Leptospirosis

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Introduction

Leptospirosis presents with a wide clinical spectrum, ranging from subclinical infection to severe multi-organ involvement. Pathogenesis involves Leptospira binding to host TLR2 receptors through LipL32, activating proinflammatory pathways (e.g., TNF-α, NF-κB), promoting immune evasion and leading to acute tubular necrosis and hepatic injury. In March 2025, a 51-year-old male farmer was hospitalized after a one-week history of fever with chills, jaundice, and anuria. Laboratory tests revealed severe hepatic and renal dysfunction, along with elevated inflammatory markers (Table 1). Given his occupational exposure and clinical presentation, Weil's syndrome—a severe manifestation of leptospirosis—was suspected and later confirmed via serological testing.

Methods

Empirical broad-spectrum antibiotic therapy (ceftriaxone, meropenem, linezolid) was initiated and subsequently de-escalated to a cephalosporin upon confirmation of the diagnosis.

Renal ultrasound showed findings consistent with acute tubular necrosis, including hypoechoic pyramids and a hyperechoic cortex, with normal kidney size.

The patient was admitted to the ICU and initiated on Continuous Kidney Replacement Therapy (CKRT), specifically Continuous Veno-Venous Hemodiafiltration (CVVHDF). Two sessions using a polycarbonate filter combined with Cytosorb® adsorber cartridges were performed to manage severe hyperbilirubinemia, resulting in an initial bilirubin reduction. Due to persistent anuria and

Table 1 | From 30/3 initiation of CKRT with two Cytosorb cartridges. On 2/4, an attempt to pause Cytosorb was restart after blood tests made in the afternoon, followed by improvement of hyperbilirubinemia. On 16/4, the patient was weaned off dialysis support during the polyuric phase

	30/3	31/3	1/4	2/4 h 7:00	2/4 h 16:00	3/4	16/4	28/4
Blood purification modality/ membrane	CVVHDF/ PCTE +Cytosorb®	CVVHDF/ PCTE +Cytosorb®	CVVHDF/ PCTE	CVVHDF/ AN69 ST	CVVHDF/ AN69 ST +Cytosorb®	CVVHDF/ AN69 ST	-	-
WBC (x10E9/L)	14.40	12.62	14.61	19.32	21.84	28.12	5.97	6.79
Hb (g/dl)	10.4	9.5	9.9	10.0	9.6	9.3	7.8	10.1
PLT (x10E9/L)	48	39	41	65	80	89	260	338
Creatinine (mg/dl)	5.4	4.48	2.66	2.24	2.04	2.21	5.79	3.03
Urea (mg/dl)	icteric sample	icteric sample	icteric sample	icteric sample	icteric sample	icteric sample	190	62
Uric Acid (mg/dl)	6.30	5.65	3.44	-	-	2.98	10.5	7.83
CRP (mg/L)	156.0	113.0	59.0	27.9	22.1	16.8	8.4	16.9
PCT (mcg/L)	49.15	30.53	21.37	12.88	-	6.3	0.66	-
Total bilirubin (mg/dl)	32.93	28.62	26.13	33.73	39.78	35.26	4.96	4.31
Direct bilirubin (mg/dl)	25.7	24.1	22.8	25.1	30	24.0	2.4	1.7
AST (U/L)	200	139	116	111	-	76	-	-
ALT (U/L)	107	85	84	94	-	82	55	-

hypertension, a new CKRT circuit with an Oxiris® (AN69 ST) endotoxin-adsorbing filter was initiated, and later a new Cytosorb® cartridge was added.

Results

The treatment achieved initial bilirubin reduction, and the addition of a new Cytosorb® cartridge led to a marked clinical and biochemical improvement.

After four CKRT circuits and three adsorber cartridges, the patient showed progressive clinical recovery, including resolution of jaundice and a transition to the polyuric phase. Two additional intermittent dialysis sessions were required.

Conclusion

The patient was discharged with improving renal function (creatinine 3.03 mg/dL, urea 62 mg/dL) and scheduled for outpatient nephrology follow-up.

A042

Use Of CytoSorb In Weil's Disease Due To Leptospirosis Infection: A Case Report

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Introduction

Leptospirosis infection can lead to Weil's disease, characterized by severe jaundice, renal failure, and hemorrhage. Mortality rates can reach up to 50% in the most severe cases. Adsorption filters may be used to reduce serum bilirubin levels.

Methods

We report the case of a 52-year-old male farmer from the Ligurian hinterland who presented to the emergency department with abdominal pain, fever, jaundice, and cognitive disturbances (agitation, flapping tremor, and hallucinations). He had experienced gastrointestinal symptoms for approximately one week. An Infectious Disease Consultant evaluated him, and he was started on antibiotic therapy with Ceftriaxone 2 g/day for suspected Weil's disease. He was transferred to our hospital due to severe jaundice and renal failure (bilirubin 32.93 mg/dL, AST 139 U/L, ALT 113 U/L, creatinine 4.97 mg/dL). Dialysis treatment was initiated using continuous veno-venous hemodiafiltration (CVVHDF) anticoagulated with calcium-citrate, utilizing CytoSorb filters for a total of three dialysis cycles, each lasting 24 hours. The patient underwent a total of 18 days of continuous renal replacement therapy (CRRT).

Results

Following treatment with CytoSorb, we observed a rapid decrease in bilirubin levels [Fig. 1] and an improvement in neurological status. CRRT was continued intermittently due to residual renal failure. On day 19, the patient was transferred to the Infectious Disease Unit for inpatient care. By day 29, the patient was discharged home with normal renal function and bilirubin levels.

Conclusion

The early implementation of CRRT with CytoSorb filters proved to be an effective intervention for managing hyperbilirubinemia associated with infectious diseases, as demonstrated in this case. This approach not only facilitated a rapid reduction in bilirubin levels but also contributed to significant neurological recovery and overall patient stabilization. These findings suggest that CytoSorb filters can be a valuable addition to the therapeutic strategies for severe cases of hyperbilirubinemia.

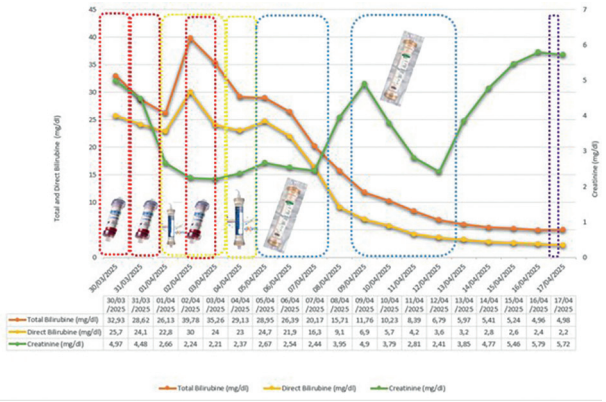

Figure 1 | 18 days of continuous renal replacement therapy (CRRT), utilizing CytoSorb for a total of three dialysis cycles, each lasting 24 hours

Liver Failure

A043

Preoperative Cytosorb "Bridge" Therapy For Jaundice Due To Direct Hyperbilirubinemia In Pancreatic Head Cancer

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Intensive Care Department of the IRCCS Hospital, Castellana Grotte, Italy

Introduction

Severe hyperbilirubinemia in patients with pancreatic cancer can increase the risk of perioperative complications, including liver failure, infections, and coagulation disorders. Conventional strategies for bilirubin reduction include endoscopic or percutaneous biliary drainage. However, in cases where these methods are not sufficiently effective, the use of Cytosorb represents an innovative therapeutic option.

Cytosorb is the only certified adsorber for the removal of bilirubin, cytokines, myoglobin, Ticagrelor, and Rivar-

oxaban from whole blood and can lead to a significant improvement in clinical parameters.

Methods
A patient diagnosed with pancreatic head cancer had previously undergone endoscopic retrograde cholangiopancreatography (ERCP) with stent placement in the main bile duct (MBD) for biliary drainage. Despite the procedure, persistent hyperbilirubinemia was observed.

Blood tests showed a total bilirubin level of 27.62 mg/dL and direct bilirubin of 24.16 mg/dL, while renal function was within normal limits.

Due to persistent jaundice and the need for preoperative bilirubin reduction, the patient underwent a Cytosorb treatment cycle (two sorbents over 48 hours).

Results
Cytosorb treatment resulted in an intense reduction in bilirubin levels: total bilirubin level reaches the value of 15.98 mg/dL and direct bilirubin reaches the value of 14.13 mg/dL after adsorption (Figure 1).

This reduction was sufficient to allow the patient to successfully undergo a duodenopancreatectomy the day after sorbent use.

Conclusions
In the case described, two Cytosorb cycles effectively reduced total and direct bilirubin levels, facilitating surgery under optimal conditions.

Cytosorb treatment proved useful for bilirubin removal in patients with severe jaundice. Cytosorb represents an effective option for the preoperative management of jaundice in patients with pancreatic head cancer.

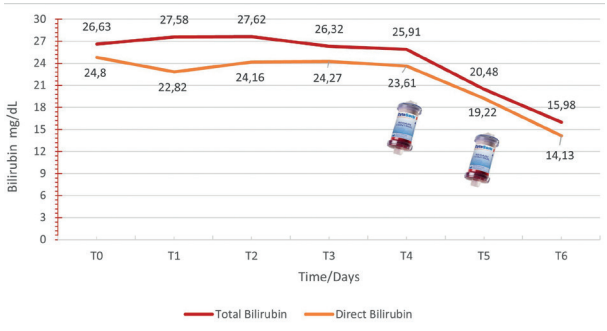

Figure 1 | Total and direct bilirubin levels

In cases where biliary drainage is insufficient, this method can improve the patient's metabolic profile and optimize surgical outcomes.

A044

Efficacy Of CytoSorb® In The Treatment Of Hyperbilirubinemia In Autoimmune Cholestatic Liver Disease

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Introduction
Extracorporeal circulation techniques can support the liver in its detoxification function, removing toxic molecules of hepatic origin such as Bilirubin and Bile Acids from the blood. Cytosorb® represents first choice purification system for this therapeutic purpose.

Methods
We report the case of a 52-year-old patient, affected by Adenocarcinoma of the right lung with secondary lung, lymph node and brain lesions, treated with Cisplatin, Pemetrexed, Ipilimumab and Nivolumab. After the third cycle of therapy, hypertransaminasemia appeared (GOT 304 U/L, GPT 651 U/L, GGT 1347 U/L), hyperbilirubinemia (TBil 6.1 mg/dL, Dbil. 4.36 mg/dL) and jaundice with positive autoantibodies (ANA 1:160 anti-SSA granular pattern) for which cortisone therapy was started. Liver biopsy showed findings compatible with DILI (Drug induced Liver Injury) with a cholestatic imprint. The patient came to our attention when, due to a progressive increase in bilirubinemia, apheresis treatment in an intensive care setting was indicated. The patient was awake and cooperative, frankly jaundiced, breathing

spontaneously in room air, hemodynamic stability without amine support.

Results
Blood tests: Tbil 25.04 mg/dL, Dbil 14.94 mg/dL, GOT 290 U/L, GPT 627 U/L, GGT 2265 U/L. An extracorporeal purification treatment in continuous hemodiafiltration (CRRT) with Cytosorb® was chosen. Treatment with Cytosorb® was carried out for 24 hours and showed an effective and progressive reduction in the values of Tbil and Dbil compared to the initial values (Tbil 16.52 mg/dL, Dbil 7.48 mg/dL). No adverse events were observed during the entire extracorporeal purification cycle.

Conclusions
The present case demonstrates the efficacy of Cytosorb® in reducing Bilirubin levels in cholestatic liver disease, with a trend that reflects the functioning of Cytosorb®, which has a concentration-dependent absorption capacity, which allows the target molecules to be effectively removed in the presence of high concentrations.

A045

The Use Of Extracorporeal Hemadsorption With CytoSorb In Liver Failure: A Case Report

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Introduction
During liver failure, various potentially toxic molecules are released into the patient's bloodstream (1).

These molecules mainly include bilirubin, ammonia and bile acids (2).

Extracorporeal treatment with Cytosorb® allows the direct removal of these hydrophobic molecules, up to 55 kDa, from whole blood, potentially preventing organ dysfunction (3,4,5,6).

Methods
A 44-year-old patient presented with jaundice for about 10 days, without abdominal pain, acholic stools, pruritus, nausea, weight loss and with no ongoing treatment for chronic diseases.

One month prior to hospitalization, the patient was evaluated in ER for chest pain, which was negative for cardiovascular diseases. Concurrently, elevated transaminase and bilirubin levels were noted. Nine days before hospitalization, the patient returned to the ER due to persistent symptoms, with a bilirubin level of 16.12 mg/dL. An abdominal ultrasound showed a heterogeneous liver with marked dilation of intrahepatic bile ducts, a contracted gallbladder, and a suspicion of neoplasm.

During hospitalization, the patient's liver condition gradually worsened, with the development of hyperammonemia (132 µMol/L) and hyperbilirubinemia (23.19 mg/dL).

Endoscopic Retrograde Cholangio Pancreatography therapy was unsuccessful and the INR significantly increased.

Consequently, a treatment with Cytosorb® and CRRT was initiated (blood flow at 100 ml/min).

Results
After 4.5 hours of treatment with Cytosorb®, the total bilirubin level decreased from 23.23 mg/dL to 17.16 mg/dL.

After 11 hours, it decreased further to 14.59 mg/dL, and the ammonia level dropped from 132 µMol/L to 37.3 µMol/L. Cytosorb® therapy was continued with a second sorbent (19 hours after the first).

10 hours after the second sorbent, the bilirubin level dropped to 9.61 mg/dL.

After 24 hours, the total bilirubin level was 9 mg/dL, and the ammonia level was 36 µMol/L and Cytosorb therapy was stopped (Figure 1).

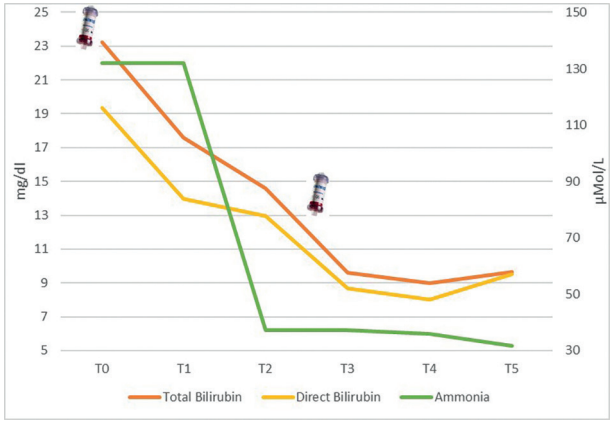

Figure 1 | Total and direct bilirubin levels, Ammonia level during CytoSorb therapy (T0: First Cytosorb, T1: After 4.5 hours of Cytosorb, T2: After 11 hours of Cytosorb, T3: After 10 hours from the second Cytosorb, T4: After 12 hours from the second Cytosorb, T5: After 24 hours from the second Cytosorb)

Conclusion

Cytosorb® is effective in removal of bilirubin and ammonia in liver failure and therefore can be a valuable liver support (7).

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A046

CytoSorb® As A Therapeutic Option In Liver Dysfunction And Mixed Jaundice Due To Drug Abuse

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Introduction

Drug and substance abuse, including the use of androgenic and anabolic steroids, remains a significant medical concern, particularly in relation to liver disease. The liver is highly vulnerable to damage from various substances, and steroid use has been specifically linked to several forms of liver injury.

Methods

Here we present a Clinical Case Report of a Liver Damage Due to Drug Use in a 26-Year-Old Male, presenting Jaundice and liver dysfunction. The patient has a history of drug abuse, including anabolic steroids and narcotics. He was using a combination of substances which were contributing to mixed jaundice and liver damage. The patient presented with yellowing of the skin and sclera. He was noted to be bradycardic, with a heart rate of 50 bpm, though he had normal renal function. The liver function tests (LFTs) revealed significant abnormalities, indicating severe liver damage (Total Bilirubin (TB): 42.20 mg/dL; Direct Bilirubin (DB): 28.82 mg/dL. The elevated direct bilirubin suggests a cholestatic component to the liver injury. SGOT (AST): 63 U/L).

Results

The patient required seven consecutive CytoSorb® treatments to successfully reduce and stabilize his TB and DB levels (fig.1), which were initially elevated to critical levels. This approach allowed for continuous liver support during the critical period of liver injury caused by the use of multiple drugs, including anabolic steroids and narcotics. In addition to reducing bilirubin, the liver function parameters were kept low during treatment,

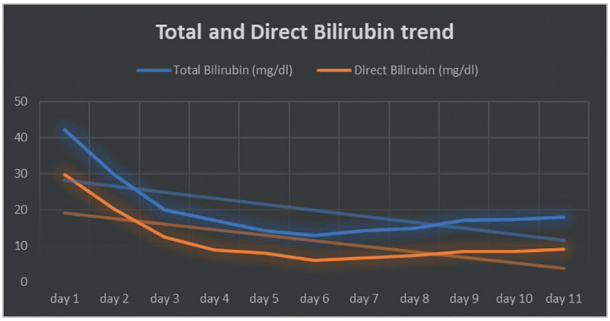

Figure 1 | Total and direct Bilirubin trend

which allowed the liver to rest and gradually begin the process of self-recovery.

Conclusion

CytoSorb® is a valuable therapeutic option for managing liver dysfunction in various conditions, including mixed jaundice associated with drug-induced liver damage. This extracorporeal blood purification therapy has demonstrated effectiveness in reducing key toxins such as TB and DB, which are central to liver dysfunction and jaundice.

A047

Continuous 48-Hour CytoSorb® Treatment In Multi-Organ Failure, Hyperbilirubinemia, And Haemolytic Anaemia In A Patient With Alcoholic Liver Disease

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Introduction

Chronic alcohol abuse is associated with multisystem complications, including hepatic dysfunction, metabolic imbalances, and neurological syndromes such as Wernicke's encephalopathy. In critically ill patients, it often presents with acute decompensation due to severe dehydration, acidosis, and heightened susceptibility to infections and drug toxicity. These factors can precipitate in systemic inflammation and multi-organ failure. In such settings, haemolytic anaemia—whether drug-induced or secondary to underlying fragility—can further compromise hepatic clearance of bilirubin, leading to severe hyperbilirubinemia. CytoSorb® hemoadsorption therapy is an emerging extracorporeal technique used in intensive care to reduce circulating inflammatory mediators and bilirubin, particularly when conventional liver or renal support is insufficient.

Methods

A female patient with a history of severe alcoholism, benzodiazepine abuse, and prior psychiatric hospitalizations was admitted to the ICU on September 19, 2024, for acute confusion, metabolic acidosis, and dehydration. On September 23, a sudden increase in serum bilirubin (5.04 mg/dL) in association with signs of acute haemolysis prompted the initiation of continuous veno-venous hemodiafiltration (CVVHD) in combination with CytoSorb® hemadsorption therapy. The primary goals were to reduce bilirubin levels and control systemic inflammation. Daily bilirubin and C-reactive protein (CRP) levels were recorded to assess treatment efficacy. A total of 4 hemadsorption cycles were administered.

Results

Following CytoSorb® initiation, bilirubin levels decreased rapidly—from 5.04 mg/dL on September 23 to 2.38 mg/dL on September 24, and then to 1.24 mg/dL by September 28. CRP levels similarly declined from 151.4 mg/L on September 23 to 29.7 mg/L by September 26. Family-reported suspicion of glucose-6-phosphate dehydrogenase (G6PD) deficiency on September 26 led to the immediate discontinuation of levofloxacin, a likely haemolytic trigger. Continued blood transfusions, metabolic support, and the cessation of the offending agent facilitated recovery of renal function, glycaemic balance, and respiratory status.

Conclusions

In this case of acute haemolytic anaemia complicating a background of chronic alcohol-related disease, CytoSorb® hemoadsorption significantly contributed to the rapid improvement of hyperbilirubinemia and systemic inflammation. Its timely use played a key role in the patient's stabilization and supported the recovery of organ function during a critical phase of illness.

A048

Observational Study About Hepatic Toxins Kinetic And Evaluation Of Organ Damage In Acute On Chronic Liver Failure (ACLF) Patients. The BILIVER Study: preliminary Results

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Introduction

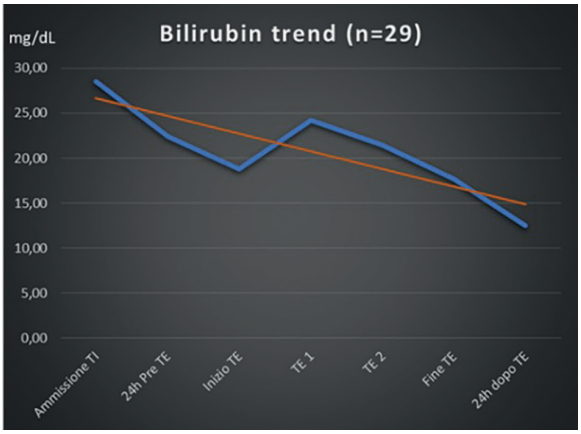
Acute on Chronic Liver Failure (ACLF) is a critical and complex condition that occurs in patients with pre-existing chronic liver disease. The European Association for the Study of the Liver (EASL) definition of ACLF describes it as an acute deterioration of liver function, often triggered by one or more acute events. This deterioration not only affects liver function but also leads to multi-organ failure, affecting extrahepatic organs and contributing to a significantly high 28-day mortality rate (>15%).

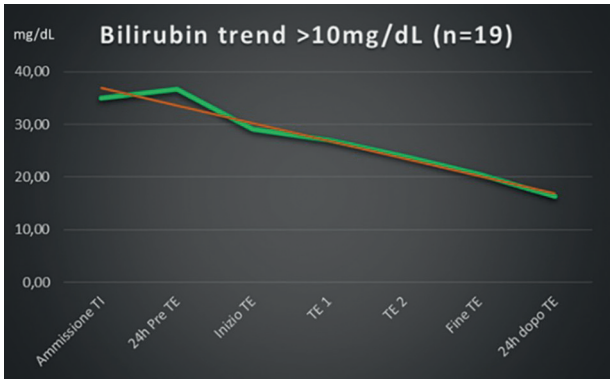
Methods

Here we present the preliminary results of an OBSERVATIONAL STUDY ABOUT HEPATIC TOXINIS KINETIC AND EVALUATION OF ORGAN DAMAGE IN ACUTE ON CHRONIC LIVER FAILURE (ACLF) PATIENTS (BILIVER study). This is a prospective, observational, non-interventional, multicenter study that aims to evaluate the outcomes of adsorption treatment in patients with Acute on Chronic Liver Failure (ACLF). The primary treatment being evaluated in the study is hemoadsorption therapy using Cytosorb, designed to remove toxins which are central to the pathogenesis of ACLF and multi-organ failure.

Results

Primary objective of BILIVER study is to evaluate how the levels of key toxins involved in liver failure—namely bilirubin, bile acids, and ammonium—change over time in patients with ACLF. In the first analysis of 29 patients, the study found that Cytosorb therapy led to a very strong trend of reduction in bilirubin levels (see fig. 1). This is an encouraging result, as bilirubin reduction suggests that hemoadsorption with Cytosorb may help to mitigate one of the key signs of liver failure, specifically the accumulation of bilirubin.





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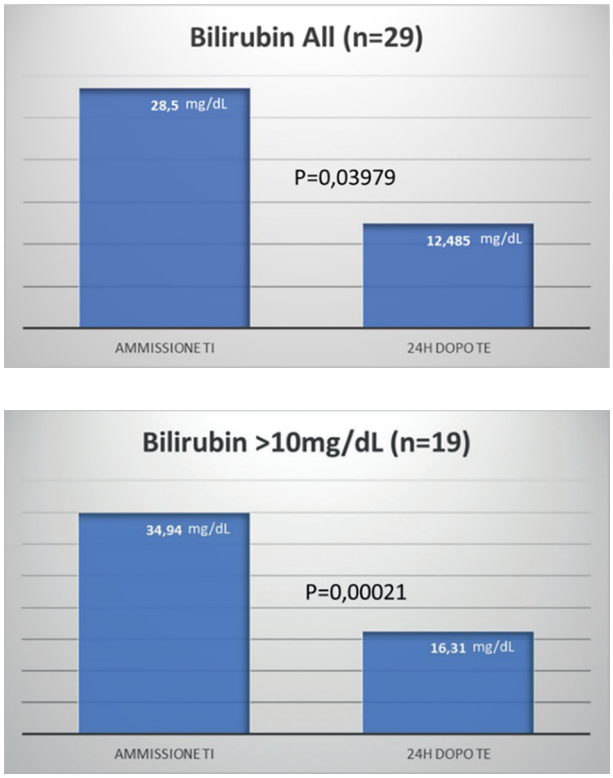

Figure 1 | Bilirubin trend for all 29 patients and for a subgroup of 19 patients with an initial bilirubin level > 10 mg/dL

Conclusions

This study is the first to demonstrate that **CytoSorb sorbent**, an **adsorptive blood purification system**, can lead to **significant reductions in bilirubin levels** in patients with ACLF. The implications of this are potentially far-reaching, as bilirubin reduction has been linked to **clinical improvements** in several critical areas.

A049

Hemoadsorption In Acute-On-Chronic Liver Failure: Impact On Hemodynamics, Organ Function, And Clinical Outcomes. Some Preliminary Results From The BILIVER Study

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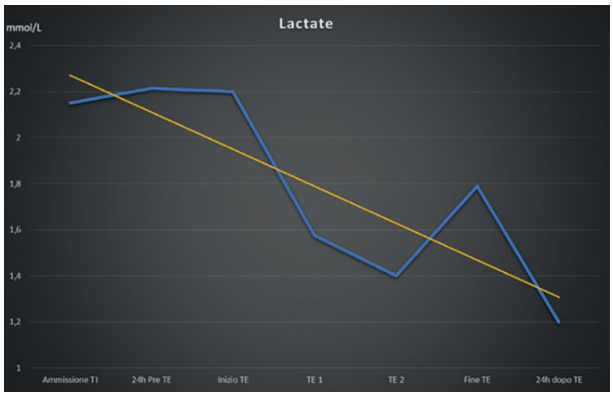
Introduction

Although the exact pathophysiology of ACLF has not yet been fully elucidated, the precipitating factor may not act directly on the liver but instead exert systemic effects. This triggers a systemic inflammatory response syndrome (SIRS), ultimately leading to single or multiple organ failure. In the most severe cases, patients may develop sepsis or even septic shock. Similar to what occurs in sepsis, the host response to the precipitating factor—by inducing hyperactivation of the immune system—creates the conditions for organ dysfunction, which, if the clinical picture persists, may progress to overt organ failure.

Methods

Here, we present some of the secondary endpoints as part of a preliminary analysis from an observational study on the kinetics of hepatic toxins and the assessment of organ damage in patients with Acute-on-Chronic Liver Failure (ACLF) (BILIVER study). As previously mentioned, many of these endpoints are associated not only with



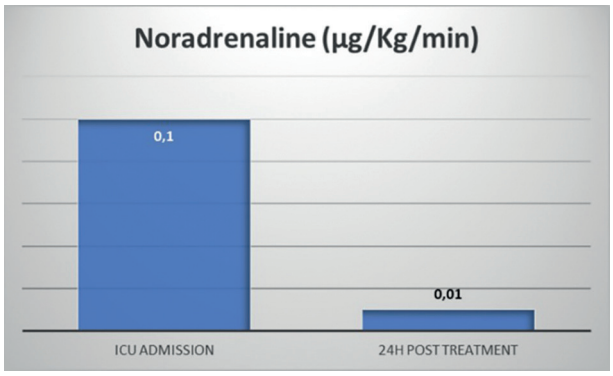


Figure 1 | Lactate trend and noradrenaline values over the treatment period

hepatic function but also with the hemodynamic consequences of ACLF. In this analysis, we evaluated the trends in noradrenaline requirements, lactate levels, MELD score and mortality.

Results

In the initial analysis of 29 patients, the study observed that CytoSorb therapy was associated with a trend toward reduced lactate levels and decreased noradrenaline requirements (see Fig. 1). Additionally, the MELD score showed an overall reduction in the study population, from a median of 39 pre-treatment to 37 post-treatment, with the most pronounced improvement observed in the subgroup of the most critically ill patients, where the score decreased from 51 to 40.5. The 90-day mortality rate was 45%, which is lower than the 53% predicted based on MELD score.

Conclusion

The use of hemoadsorption in patients with ACLF may not only contribute to a reduction in bilirubin levels, but may also positively impact the hemodynamic profile, potentially improving organ function and overall outcomes.

A050

Baseline Characteristics Of 29 Patients With ACLF ≥2: Interim Analysis Of The BILIVER Study

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Introduction

Several extracorporeal liver support systems have been developed and tested to manage ACLF. CytoSorb has recently been introduced. The role of these extracorporeal therapies in the management of ACLF remains to be fully elucidated.

Methods

This is an interim analysis of baseline characteristics from 29 patients enrolled in BILIVER study. All patients met diagnostic criteria for ACLF≥2 and were admitted to the ICU for various clinical indications. Demographic, clinical, and laboratory parameters were collected at the time of enrollment.

Results

We analyzed a cohort of 29 patients diagnosed with Acute-on-Chronic Liver Failure (ACLF≥2), associated with various underlying liver disease: 48% of cases were virus-related, 21% were alcohol-related, and 31% were due to other causes such as drug-induced liver injury (e.g., NSAID overuse), or triggers as hepatotoxic agents and gastrointestinal hemorrhage. The median weight was 80 kg (IQR 60–91 kg) and the median age was 55 years (IQR 49–65 years). At ICU admission, patients had a median SOFA score of 13.5 (IQR 10–16), a median CLIF-C ACLF score of 3 (IQR 2–4), and a median MELD score of 39 (IQR 33–49). All patients were admitted to

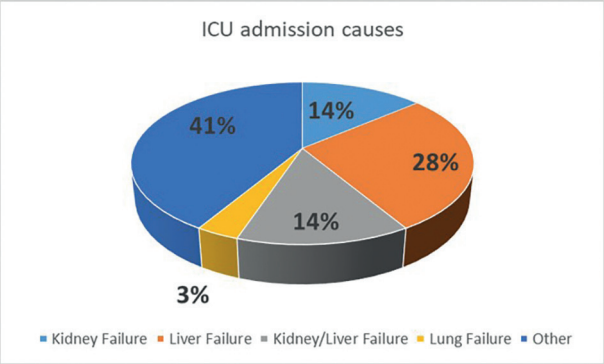

Figure 1 | ICU admission causes in the first 29 ACLF≥2 patients enrolled in BILIVER study

the ICU for ACLF≥2, but the immediate cause for admission varied: 14% due to acute kidney injury, 28% due to hepatic failure, 14% due to a combination of both, and 41% for other reasons—of whom 67% were admitted with multiorgan failure (MOF) or septic shock (see figure 1). Multiple patients had relevant comorbidities, most frequently arterial hypertension, type 2 diabetes mellitus and obesity.

Conclusion

The underlying hypothesis of this study is to assess whether modulation of bilirubin levels and other toxic molecules and inflammatory mediators, achieved through the use of extracorporeal blood purification systems, may have a therapeutic impact in patients with ACLF≥2.

A051

Cytosorb® Hemoadsorption As Metabolic Prehabilitation In Hepato-Biliary Sepsis: A Case Of Post-ERCP Pancreatitis With Severe Hyperbilirubinemia

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Introduction

CytoSorb® is an extracorporeal hemoadsorption device designed to reduce circulating cytokines and endogenous toxins such as bilirubin. While its role in septic shock is increasingly recognized, emerging applications include organ support in patients with hepatic dysfunction, potentially serving as a metabolic bridge to surgery.

Methods

We report the case of a critically ill patient admitted to the ICU with severe post-ERCP pancreatitis complicated by septic shock and multi-organ failure. The ERCP was performed for biliary decompression in the setting of a malignant biliary obstruction. The patient presented with extreme hyperbilirubinemia (>20 mg/dL), which constituted a major contraindication for curative surgical intervention due to the high perioperative risk.

CytoSorb® therapy was initiated in combination with continuous renal replacement therapy (CRRT), with the dual objective of modulating the systemic inflammatory response and reducing bilirubin levels. Within 48 hours,

bilirubin levels declined significantly and inflammatory markers improved, indicating a favorable metabolic response.

Results
Regardless of patient outcome, the biochemical and hemodynamic improvement and the rapid decline in bilirubin suggests that CytoSorb® may offer a viable strategy for metabolic prehabilitation in selected patients with hepatic impairment, potentially increasing surgical eligibility and improving outcomes.

Conclusion
This case illustrates the potential role of CytoSorb® hemoadsorption as an adjunctive therapy for metabolic optimization in critically ill patients with hepatic dysfunction. As a bridge-to-surgery or component of a prehabilitation strategy, it may enhance the feasibility of curative procedures in otherwise inoperable patients. This case supports the need for further investigation into the role of extracorporeal therapies as tools for metabolic optimization and preoperative conditioning in high-risk hepatobiliary patients.

A052

Use Of CytoSorb In The Management Of Hyperbilirubinemia In A Patient With Suspected Hemophagocytic Syndrome And Autoimmune Cholestatic Hepatitis

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Introduction
CytoSorb has been shown to effectively reduce bilirubin and bile acid levels in patients with liver dysfunction. This approach may also aid in the management of hyperbilirubinemia in patients with hemophagocytic syndrome and autoimmune cholestatic hepatitis, providing supportive therapy alongside immunosuppressive and surgical interventions.

Methods
A 67-year-old male presented to the emergency department with acute respiratory failure, pulmonary infiltrates, jaundice, and pancytopenia. Initial investigations revealed acute liver dysfunction with markedly elevated total bilirubin (TB: 20.8 mg/dL). Serology showed minimal Epstein-Barr virus (EBV) reactivation, deemed unrelated to the clinical picture. A hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) was suspected. Liver biopsy was compatible with post-acute cholestatic hepatitis of autoimmune etiology, and high-dose corticosteroid therapy was initiated.

Results
Due to the severity of hyperbilirubinemia and risk of worsening liver failure, the patient underwent a 24-hour CytoSorb hemoadsorption session, resulting in a rapid reduction of bilirubin levels. The following day, the patient underwent splenectomy to address persistent pancytopenia and suspected hemophagocytic activity. However, three days postoperatively, a significant rebound in bilirubin and liver enzymes (ALT, AST, GGT, LDH, ALP) was observed. A second CytoSorb session, lasting 16 hours, was initiated with favorable results: bilirubin levels dropped progressively, reaching 1.95 mg/dL, and liver function parameters stabilized or improved

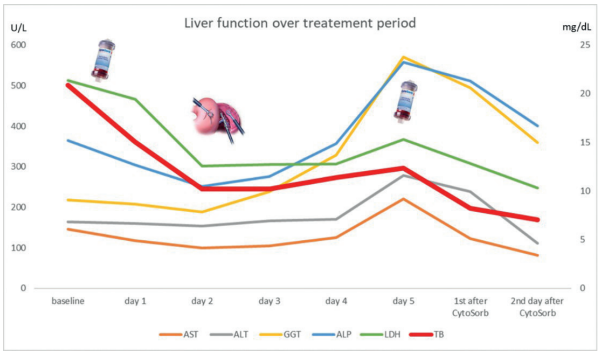

Figure 1 | Liver function parameters over treatment period

(see figure 1). The patient's liver profile remained stable through hospital day 29, at which point he was discharged in good clinical condition.

Conclusion

This case highlights the potential role of CytoSorb hemoadsorption therapy as an adjunctive treatment for severe hyperbilirubinemia in the setting of acute liver dysfunction and suspected HLH. The therapy was effective in rapidly reducing bilirubin levels and improving liver function parameters, both pre- and post-splenectomy. Further studies are warranted to evaluate the broader application of hemoadsorption in immune-mediated liver pathologies and HLH-like syndromes.

A053

CytoSorb Hemoadsorption As A Bridging Strategy In Acute Liver Failure: A Narrative Review

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Introduction

Acute liver failure (ALF) and acute-on-chronic liver failure (AoCLF) are life-threatening syndromes marked by impaired detoxification, coagulopathy, and multiorgan dysfunction. Accumulation of protein-bound toxins such as bilirubin and myoglobin exacerbates systemic inflammation and organ failure. While liver transplantation remains the definitive treatment, extracorporeal blood purification methods have emerged as effective bridging therapies. Among these, CytoSorb® has shown to be effective in removing hydrophobic molecules such as cytokines, bilirubin, and myoglobin from whole blood. Its potent adsorptive capacity helps to mitigate systemic toxicity, reduce cytokine storm intensity and improve hemodynamic stability in critically ill patients, potentially enhancing survival chances.

Methods

Recent clinical experiences have highlighted the use of CytoSorb in critically ill patients with acute liver failure (ALF) and associated complications such as hepatorenal syndrome and multiorgan dysfunction. In these scenarios, extracorporeal blood purification (particularly continuous veno-venous hemodialysis (CVVHD) integrated with CytoSorb) has been successfully employed as a bridging therapy to liver transplantation. Treatment is typically initiated upon ICU admission in patients presenting with severe hyperbilirubinemia, acute kidney injury, coagulopathy, and signs of neurological and respiratory compromise. Scoring systems such as APACHE IV often indicate high predicted mortality.

Results

CytoSorb therapy has been associated with a progressive and clinically meaningful reduction in circulating bilirubin and myoglobin, contributing to enhanced detoxification and modulation of the inflammatory response. Clinical improvements include reduced vasopressor needs, better hemodynamic stability, and improved metabolic profile supporting organ recovery. The integration of CytoSorb into CRRT platforms has proven technically straightforward, safe, and well tolerated. These findings suggest CytoSorb as a valuable and effective bridge-to-transplant tool in patients with ALF and multiorgan failure, improving short-term outcomes.

Conclusion

CytoSorb represents a promising adjunct in managing hyperbilirubinemia and hypermyoglobinemia in liver failure. By adsorbing protein-bound toxins and inflammatory mediators, CytoSorb contributes significantly to organ stabilization and improved outcomes, especially in high-risk patients awaiting transplantation. Its compatibility with CRRT platforms, prolonged adsorptive capacity, ease of use, and safety profile support broader ICU application.

A054

Intraoperative Continous Kidney Replacement Therapy (CKRT) Use During Liver Transplantation

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Introduction

Liver transplantation (LT) is often associated with acute perioperative complications such as massive hemorrhage, hemodynamic instability, and electrolyte or acid-base disturbances. These factors can contribute to the development of acute kidney injury (AKI). In this context, continuous kidney replacement therapy (CKRT) may offer several advantages, including removal of water-soluble toxins (e.g., ammonium), correction of electrolyte imbalances, prevention of fluid overload, and management of intracranial hypertension.

Although CKRT is commonly employed in the perioperative setting, its intraoperative use remains relatively rare and less well documented.

Methods

In 2024, intraoperative CKRT was performed in 3 out of 41 LT procedures (7.3%) at our center due to concomitant hepatorenal dysfunction.

A Fresenius Multifiltrate monitor was used in CVVHD mode with Multibic dialysate. Anticoagulation was managed either with heparin/protamine per institutional protocol (n=2) or omitted altogether (n=1) (Table 1). Timing of CKRT initiation was decided in coordination with the anesthesiology team: in one case, treatment began at anesthesia induction, while in the other two, it started post-hepatectomy.

Jugular venous access was used in all cases. The intraoperative duration of CKRT ranged from 6 to 8 hours. All patients remained hemodynamically stable, and no treatment-related complications were observed. Two patients continued dialysis in the postoperative period, including one who was already on chronic dialysis.

Results

All three patients were alive at 30 days post-transplant. One patient died two months after LT due to infectious complications; another died four months postoperatively due to intestinal perforation.

Table 1 | Example of Intraoperative CKRT Prescription during Liver Transplantation (Local Experience)

Monitor	FRESENIUS Multifiltrate®
Dialysate Bags	MULTIBIC®
Mode	CVVHD
Filter	AV1000 EMIC2
Qb	80-100 ml/min
Qd	1500-2000 ml/h
Anticoagulation	- no one - heparin/protamine according to internal protocol: 1 cc of heparin (5000 U) antagonized by 1 vial (50 mg/5 ml) of protamine. For example: -Pre-filter: 5 cc of heparin (25000 U) in 100 cc of NS at 4 ml/h -Post-filter: 5 vials of protamine (250 mg) in 100 cc NS at 4 ml/h
Vascular Access	- Hemodialysis CVC - 2 single-lumen central venous infusion catheters (1 for inflow, 1 for outflow)

Conclusion

Intraoperative CKRT during LT appears to be a feasible and safe intervention. It supports hemodynamic stability, fluid balance, and correction of acid-base and metabolic disturbances, potentially reducing complications and contributing to a safer surgical course in complex transplant cases.

Rhabdomyolysis

A055

Rosuvastatin-Ticagrelor Induced Rhabdomyolysis – A Case Report On The Role Of Cytosorb® Haemoadsorption

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Introduction

Drug interactions between rosuvastatin and ticagrelor can lead to clinically significant rhabdomyolysis. This risk is amplified by factors like drug-drug interactions (especially with medications metabolized by the cytochrome P450 system), genetic predispositions, and advanced age, common in acute coronary syndrome patients. Ticagrelor, a P2Y12 inhibitor, is known to interact with statins. This case report specifically explores how ticagrelor and rosuvastatin can cause rhabdomyolysis and subsequent Acute Kidney Injury (AKI).

Case Report

We present the case of a 71-year-old woman affected by cardiovascular history (in 2019, primary percutaneous transluminal angioplasty (PTA) with drug-eluting stent placement for an anterior STEMI, continuing dual antiplatelet therapy with ASA and ticagrelor due to subsequent in-stent restenosis); in addition, her lipid-lowering therapy was optimized by replacing atorvastatin with rosuvastatin. Six months prior to her current admission, her kidney function was normal. She was admitted to the ER, with significant bilateral lower limb weakness, myalgia, difficulty walking, appetite loss, diarrhea, and fever; AKI was diagnosed, with severe alterations of renal function (serum creatinine 11.03 mg/dL, serum urea 406 mg/dL) and metabolic acidosis. Moreover, significant elevations in CPK (84711 U/L) and Myoglobin (25406 ng/mL) were documented. She received fluid therapy and a Continuous Renal Replacement Therapy (CRRT) in CVVHDF modality coupled with Cytosorb®, was initiated early after the nephrology admission. Cytosorb® cartridges were sorbent replaced every 24 hours with a significant reduction in CPK and myoglobin in the following 72h (Figure 1) and a significant improvement of kidney function, leading to CRRT discontinuation (Figure 2). Her medications were adjusted to clopidogrel and alirocumab, and she gradually returned to her baseline kidney function within a month.

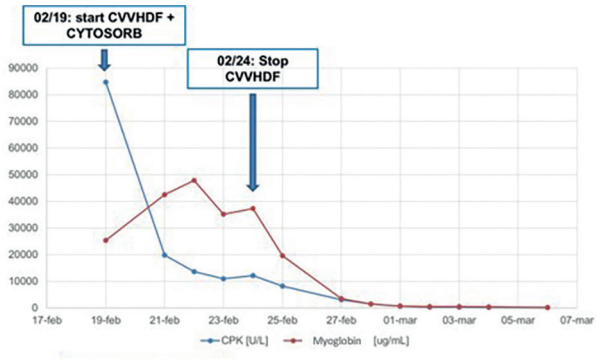

Figure 1 | CPK and Myoglobin trends

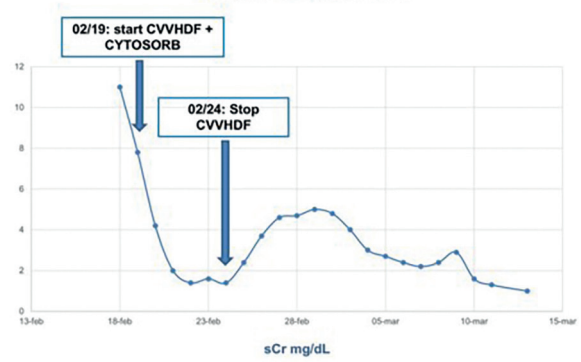

Figure 2 | Creatinine trend

Conclusions

The interaction between rosuvastatin and ticagrelor appears multifactorial. Hemoadsorption with CytoSorb® is effective in adsorbing myoglobin and removing ticagrelor, representing therefore an important therapeutic option for ticagrelor-rosuvastatin induced rhabdomyolysis.

A056

Treatement Of Rhabdomyolysis-Induced AKI With Blood Purification

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Introduction

An increasing number of studies suggest the effectiveness of hemoadsorption (HA) in managing severe rhabdomyolysis. CK and myoglobin seem to be correlated, but the most studies identify myoglobin as a better biomarker and some authors suggest a limited removal of CK even with HA.

Methods

A 3-year-old girl weighing 13kg admitted to the PICU for altered sensorium, hyponatremia, metabolic acidosis, and hyperkalemia diagnosed as severe viral rhabdomyolysis. CK values increase from 33,742 to 290,980U/L within 24h. Real-time myoglobin measurement was unavailable. Continuous Kidney Replacement Therapy (CKRT) treatment was initiated using a high-flux (ANST69) continuous veno-venous hemodiafiltration (CVVHDF) mode.

Results

We observed a further increase in CK values over the next 4h, reaching a maximum of 349,600U/L. Subsequently HA with a Cytosorb in combination with CKRT was initiated with a reduction of CK to 117,200U/L in the next 6h. The sorbent was then replaced after 12h following a CK plateau at 118,640U/L. After 12h, we further changed the column and CK values reduced to 63,860U/L. Thus, we decided to continue treatment exclusively with CKRT, observing a progressive reduction in CK values to < 10.000 U/L (figure 1). The patient was discharged from the PICU on the 10th day with no dependence on dialysis.

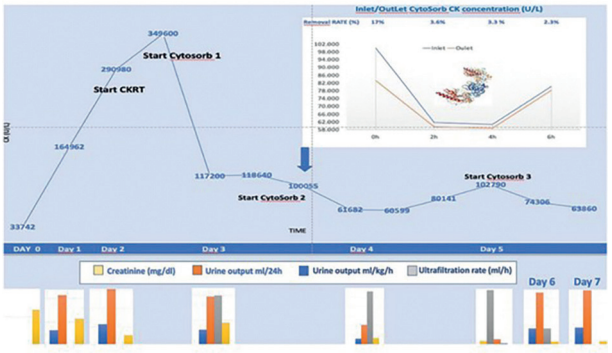

Figure 1 | Upper section of the figure shows time course of Creatinine Kinase (CK) during the extra-corporeal therapy with Continuous Kidney Replacement Therapy (CKRT) and Cytosorb hemoadsorption. The white window depicts the time course of CK measured at the inlet and the outlet of the cartridge between Time 0 (0h) and after 6h (6 h). At the different time points is reported the CK removal ratio of the cartridge (calculated as [Concentration at baseline (CB0)–Concentration at the end of the treatment (Cend)/CB0x100]). Bottom section of the figure shows the histograms ad different time points for creatinine blood level (yellow bars), urine output measured in ml in 24h (orange bars), urine output measured as mlxkg/h (blue bars), ultrafiltration rate of CKRT (ml/h)

Conclusion

we advocate for a "paradigm shift" in managing severe rhabdomyolysis, recommending HA for CK levels >12,000U/L and >10,000ng/ml myoglobin.

A057

A Novel Approach To Myoglobin Clearance And Organ Preservation In Severe Rhabdomyolysis: Dual concomitant CytoSorb Hemoadsorption Therapy

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Introduction

Severe rhabdomyolysis, characterized by extensive muscle breakdown and release of myoglobin and creatine kinase (CK), is a life-threatening condition often complicated by acute kidney injury (AKI) and multi-organ failure (MOF). Even when conventional treatments such as fluid resuscitation and renal replacement therapy (RRT) are timely applied, severe cases remain challenging to manage. Among therapies available in this setting, hemadsorption with CytoSorb has the potential not only to treat rhabdomyolysis through removal of circulating molecules but also to limit or even prevent rhabdomyolysis-related renal failure and MOF. We present preliminary data of a novel use CytoSorb hemoadsorption therapy, which encompassed the use of two CytoSorb cartridges running in parallel, to enhance myoglobin and cytokine clearance.

Methods

Retrospective case series of adult patients with massive rhabdomyolysis of heterogeneous origin treated with dual concomitant cytosorb circuits running in parallel at our institution.

Results

Clinical data from three patients with severe rhabdomyolysis were reviewed: a 26-y woman with acute ischemia and to compartment syndrome of the left leg, necessitating fasciotomy, in the context of multiple emobolization from intracardiac myxoma (fig 1A); a 54-y woman with cardio-septic shock requiring intraaortic balloon pump support and with diffuse muscular injury (fig 1B); a 41-y male with massive rhabdomyolysis due to prolonged leg ischemia in the context of type A aortic dissection who underwent emergent cardiac surgery (fig 1C). In all patients, dual concomitant CytoSorb treatments was associated with marked improvements in CK, renal, hepatic, and inflammatory marker. Potential impact on CRRT reduction could not be assessed due to the very limited sample size.

Conclusions

Dual CytoSorb therapy offers a transformative approach to severe rhabdomyolysis, with potential for organ preservation and recovery in critically ill patients. Future studies are warranted to further evaluate its efficacy and refine its application in acute multi-organ failure contexts.

Figure 1 | Temporal trend of laboratory parameters. Figures illustrate the evolution of various laboratory biomarkers over several days of monitoring. The Y-axis represents laboratory values plotted on a logarithmic scale to better visualize differences in magnitude. The X-axis indicates the days of observation

A058

Intermittent Cytosorb In Active Rhabdomyolysis: Convenient Or Non-Convenient?

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Introduction

Rhabdomyolysis is a condition characterized by the breakdown of muscle cells, releasing myoglobin, which can lead to renal damage.

Last rhabdomyolysis consensus[1] showed how hemadsorption with CytoSorb should be used as effective therapy to remove myoglobin, preventing or reducing renal damage.

Methods

An 11-year-old girl with hypokinetic dilated cardiomyopathy and homozygous mutation in the TNNI3 gene, underwent orthotopic heart transplantation following LVAD support complicated by a driveline infection. Post-transplant, she developed severe rhabdomyolysis (myoglobin 31,800 ng/ml; and CPK >28,000 U/l), along with spastic tetraparesis with areflexia. This necessitated the initiation of continuous venovenous hemodiafiltration (CVVHDF) and CytoSorb hemadsorption therapy applied on alternate days, with blood samples taken every 6 hours to monitor the severity of rhabdomyolysis.

Results

After 24 hours of hemadsorption, myoglobin levels decreased to 16,928 ng/ml and CytoSorb was stopped (Day 2). Myoglobin rose again to 25,655 ng/ml (CPK 23,739 U/l) within 24 hours, prompting a second cycle (Day 3). On day 5, persistent high myoglobin levels (13,052–9,032 ng/ml) led to the application of a third CytoSorb, reducing myoglobin to 5,456 ng/ml and CPK to 5,097 U/l. By day 7, lower CPK and myoglobin levels (4,467–4,128 U/l, 5,869–3,997 ng/ml) allowed the definitive discontinuation of CytoSorb therapy, with only CVVHDF to clear excess molecules (figure 1).

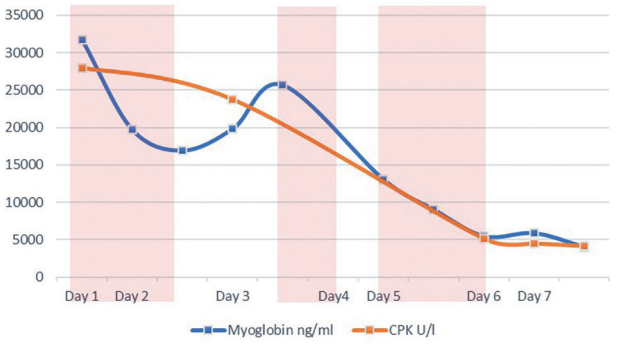

Figure 1 | Myoglobin and CPK trend during treatment

On day 11, CVVHDF was stopped, and the patient's kidney returned to normal function, with laboratory results within normal limits.

Conclusions

CytoSorb proved its effectiveness in reducing elevated levels of myoglobin and CPK; however, we observed that in cases of ongoing and active rhabdomyolysis, applying hemadsorption on alternate days may result in the accumulation of molecules, as seen in other reported experiences[2]. We conclude, in line with the latest consensus[1], that CytoSorb therapy should not be discontinued until myoglobin levels fall below 5,000 ng/ml.

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A059

Use Of Cytosorb For Treatment Of Diabetic And Pharmacological Rhabdomyolysis

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Background
Rhabdomyolysis is a condition characterized by the breakdown of muscle cells, releasing myoglobin, which can lead to renal damage. Causes include trauma, intense exercise, drugs, and conditions like infections or diabetes.

Treatment involves fluid rehydration and, in severe cases, dialysis and hemadsorption to remove toxins.

Case Report
A 21-year-old male with obesity and autism, on Risperdal (1 mg), presented to the emergency department with confusion, fatigue, tachypnea, tachycardia, and hypotension, accompanied by fever. Blood tests indicated hyperglycemia (66 mmol/L), metabolic acidosis, lactadicemia (3.6 mmol/L), and inflammation (PCT 0.96 mcg/L, WBC count 18,000/ml), alongside elevated creatinine (303 µmol/L).

Diagnosed with diabetic ketoacidosis, he was admitted to the ICU and treated with empirical ceftriaxone. As his condition deteriorated, he required vasopressors, a switch to meropenem and linezolid, orotracheal intubation, and continuous veno-venous hemodiafiltration (CVVHDF) for suspected septic nephropathy.

By day 5, his creatine phosphokinase (CPK) levels had surged to 297,880 U/L, no sources of sepsis were found, prompting a diagnosis of rhabdomyolysis triggered by diabetic ketoacidosis and Risperdal.

CVVHD with a high-cut off filter was initiated on day 7 due to persistent CPK elevation.

On day 9 Cytosorb hemadsorption was added because of high CPK and myoglobin (125212 mcg/l) levels. CPK and myoglobin levels began to decrease significantly from day 10. Treatment with CytoSorb continued for 5 days, and it was stopped when myoglobin levels were low. The measurements were made pre and post cartridge to better understand the sorbent performance (figure 1).

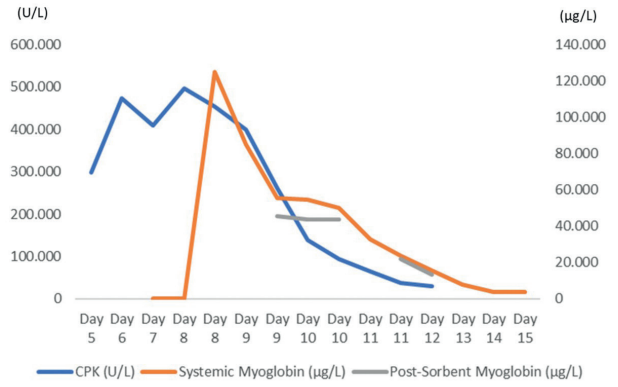

Figure 1 | CPK and Myoglobin trend during days

The patient required renal replacement therapy until day 26, was weaned from mechanical ventilation with a tracheostomy, and discharged with a GFR of 81 ml/min.

Conclusions
CytoSorb was effective in reducing high levels of myoglobin and CPK associated with severe diabetic and pharmacological rhabdomyolysis, where standard CRRT alone was insufficient.

A060

Septic Shock Associated With Severe Rhabdomyolysis In A Chronic Hemodialysis Patient Successfully Treated With CRRT And Cytosorb: A Case Report

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Introduction
Rhabdomyolysis is a clinical syndrome characterized by skeletal muscle tissue necrosis, leading to the release of substances, including myoglobin.

The most common causes include trauma, medications, drugs abuse, and infections. A definitive diagnosis is confirmed by measuring myoglobin and creatine phosphokinase (CK).

Increased myoglobin levels could lead to acute kidney injury (AKI). Several extracorporeal purification techniques have been used to treat rhabdomyolysis-induced AKI, including kidney replacement therapies, and hemadsorption with CytoSorb to accelerate the removal of myoglobin.

We describe the case of a chronic hemodialysis patient with severe rhabdomyolysis secondary to sepsis, successfully treated with continuous renal replacement therapy (CRRT) and Cytosorb.

Methods
A 78-year-old male patient with chronic kidney disease undergoing biweekly hemodialysis was admitted to the emergency department for fever and general malaise. He subsequently developed septic shock with hemodynamic instability, requiring vasopressor support, and was admitted to the intensive care unit.

Laboratory tests showed increased procalcitonin (753 ng/ml) and significantly elevated myoglobin (106,691 mcg/l) and creatine kinase (CK) (82,080 U/L), indicating rhabdomyolysis secondary to sepsis, likely originating from the hemodialysis' central venous catheter (CVC).

Continuous veno-venous hemodialysis (CVVHD) with regional citrate-calcium anticoagulation was started applying Cytosorb, and replacing the sorbent every 12 hours. The treatment continued for 72 hours.

Empirical broad-spectrum antibiotic therapy was started and adjusted based on blood culture results, which confirmed Aeromonas Jandaei infection from the CVC.

Results
After the first 24 hours of treatment, myoglobin and CK levels decreased by 80% and 76%, respectively. By the end of the full CVVHD plus Cytosorb cycle, myoglobin and CK levels further decreased to 4,565 mcg/l and 2,694 U/L, corresponding to reductions of 95% and 96%.

Progressive clinical improvement allowed for the discontinuation of CRRT, resumption of intermittent bicarbonate hemodialysis, and transfer to the internal medicine department. The patient was discharged home after 15 days of hospitalization.

Conclusions
CRRT combined with CytoSorb proved effective in rapidly reducing circulating myoglobin levels, helping to preserve diuresis and residual kidney function. Furthermore, it is hypothesized that the reduction of inflammatory cytokines, although not directly measured, may have contributed to the resolution of septic shock.

A061

Use Of Blood Purification In Rhabdomyolysis Resulted From Amputation Of Both Lower Limbs

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Introduction
Rhabdomyolysis is a serious condition that results from muscle injury, and it can indeed manifest as a result of trauma like road traffic accidents. Dialysis is often not sufficient on its own to address the problem, especially in cases with elevated myoglobin levels. Blood purification methods using sorbents can be an alternative or adjunctive treatment.

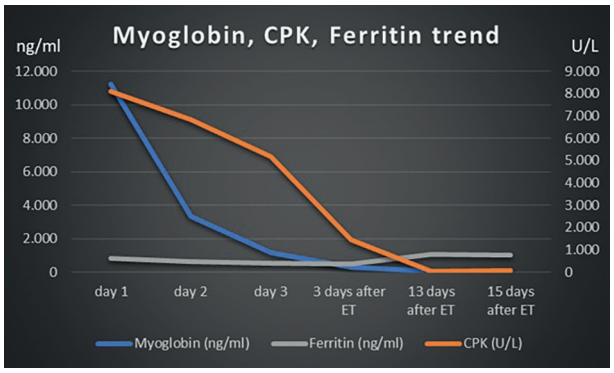

Figure 1 | Decrease of Myoglobin CPK

Methods

We describe a 54-year-old male patient who sustained severe trauma, resulting in complete amputation of both lower limbs after a road traffic accident. His immediate post-operative course, including hemodynamic instability and respiratory issues, was concerning. Given the high levels of **myoglobin**, **ferritin** and **CPK**, the decision to initiate **Continuous Renal Replacement Therapy (CRRT)** with **Cytosorb** was an appropriate one for addressing potential complications, especially **rhabdomyolysis-induced kidney injury**.

Results

The blood gas improvements (pH 7.4, PCO2 43, PO2 88, P/F ratio 1.48) suggested that respiratory function was improving. After two days of treatment, the decision to suspend CRRT was made due to the improvement in laboratory markers, showing that myoglobin and CPK levels had decreased (fig.1). This decision was based on the clinical improvement in the patient's kidney function, as reflected by normal diuresis and the decrease in toxins. After some days, despite the improvement in respiratory and renal function, the patient continued to require vasopressor. After 10 days, sedation was suspended, and weaning from mechanical ventilation was initiated. Then, antibiotic therapy was suspended. The patient's overall clinical status at this point.

Conclusion

CytoSorb has proven to be effective in cases of amputation-related rhabdomyolysis, particularly when there is a massive release of toxins like myoglobin, CPK, and ferritin. The continued effectiveness of CytoSorb even up to two weeks after treatment cessation is an important aspect, demonstrating the sustained clearance of these toxic substances and the long-term benefit of the therapy (fig 1).

A062

Cytosorb® - A case Report Hemoadsorption In Crush Syndrome–Related Rhabdomyolysis And AKI: A Case Of Rapid Clinical Stabilization With CytoSorb® And CRRT

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Introduction

Severe rhabdomyolysis, characterized by massive release of myoglobin into the bloodstream following muscle injury, represents a potentially life-threatening condition associated with acute kidney injury (AKI), metabolic disturbances, and multiorgan dysfunction. In this context, CytoSorb®, the only cartridge certified for the removal of cytokines, bilirubin, myoglobin, ticagrelor, and rivaroxaban, has proven useful in reducing the myoglobin burden, thereby mitigating renal tubular damage.

Methods

A 64-year-old male was admitted to the emergency department following a road traffic accident, presenting in a coma (GCS: 6) with massive rhabdomyolysis complicated by severe metabolic acidosis, diabetic ketoacidosis, acute respiratory failure, heart failure, and AKI.

Initial laboratory values revealed: pH: 7.30, pCO_2: 13 mmHg, pO_2: 105 mmHg, HCO_3^-: 6.4 mmol/L, Base excess: -20 mmol/L, K^+: 1.9 mmol/L, Na^+: 150 mmol/L, Blood glucose: > 300 mg/dL, Myoglobin: > 3976 ng/mL (exceeding measurement device limit).

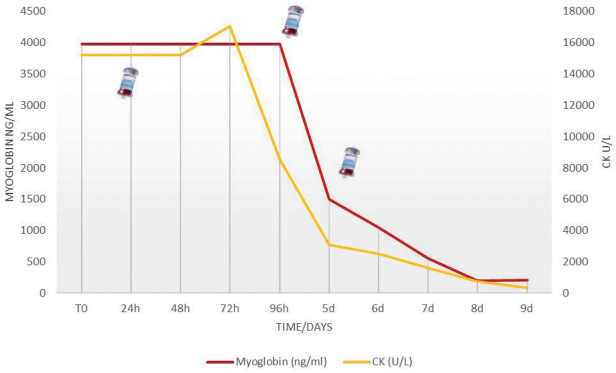

Figure 1 | Myoglobin and CK trend over treatment period

The patient underwent orotracheal intubation and mechanical ventilation. Fluid resuscitation was initiated with 8.4% sodium bicarbonate, potassium chloride, and free water via nasogastric tube, alongside hemodynamic support with vasoactive amines.

On the following day, continuous renal replacement therapy (CRRT) was started, and a first cycle of CytoSorb® hemoadsorption was applied. After a 48-hour suspension, two additional treatment cycles were performed (total of three cartridges used).

Results

Myoglobin levels decreased from >3976 ng/mL to 1046.8 ng/mL.

Creatine phosphokinase (CPK) levels dropped from 15,192 ng/mL to 2,499 ng/mL.

Serum albumin remained stable throughout the treatment period (Figure 1).

The day after completing CytoSorb® therapy, sedation was discontinued. The patient was extubated and resumed spontaneous diuresis.

Conclusions

In this complex case of crush syndrome with massive rhabdomyolysis, diabetic ketoacidosis, and multiorgan failure, the use of CytoSorb® in combination with CRRT proved effective in removing myoglobin. Early initiation of treatment helped reduce the systemic toxic burden, supporting organ recovery and the clinical stabilization of the patient.

A063

Drug-Induced Rhabdomyolysis: The Clinical Significance Of Combined Rosuvastatin And Ticagrelor Therapy And Myoglobin Clearance Via Cytosorb® - A case Report

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Introduction

Rhabdomyolysis is a clinical syndrome characterized by the release of intracellular contents -particularly myoglobin- into the bloodstream, which can lead to acute kidney injury (AKI). Drugs such as rosuvastatin, especially when combined with antiplatelet agents like ticagrelor, are a common cause of iatrogenic rhabdomyolysis. In this setting, Cytosorb®, the only cartridge certified for the removal of cytokines, bilirubin, myoglobin, ticagrelor, and rivaroxaban, has shown efficacy in reducing myoglobin burden and attenuating renal tubular damage.

Methods

A 78-year-old man with a history of hypertension, dyslipidemia, ischemic-hypokinetic-valvular heart disease and stage 3A chronic kidney disease (CKD) presented to the ED with vomiting, fatigue, diffuse myalgia, and oliguria. He was on treatment with rosuvastatin, ezetimibe, and ticagrelor.

Laboratory tests revealed stage 3 AKI, severe rhabdomyolysis (myoglobin 16,000 ng/mL, CK 6117 U/L), and marked hepatic cytolysis.

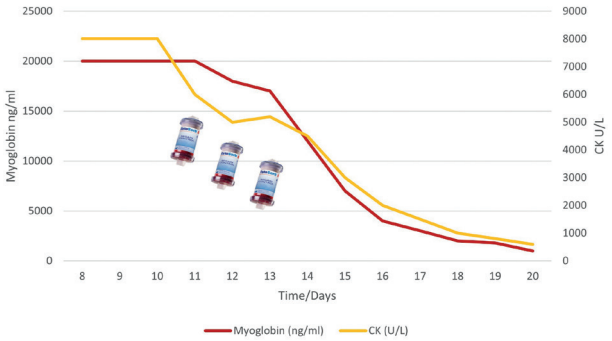

Figure 1 | Myoglobin and CK trend over treatment period

A diagnosis of statin-induced rhabdomyolysis was made, prompting immediate discontinuation of both rosuvastatin and ezetimibe. As the clinical condition persisted, the patient underwent IVVHD, followed by CVVHD using a high cut-off filter.

After 10 days of CVVHD, laboratory values showed only minimal improvement, suggesting a persistent toxic burden. Consequently, Cytosorb® therapy was initiated in combination with CRRT.

Results

Within 72 hours (3 cartridges), myoglobin levels decreased from 20,000 ng/mL to 10,000 ng/mL, and CK levels dropped from 7,500 U/L to 3,900 U/L, showing a consistent downward trend (Figure 1).

The patient continued on CRRT alone for an additional 12 days until discharge from the ICU.

Conclusions

This case highlights the importance of careful evaluation in patients with chronic kidney disease receiving potentially interacting drugs such as rosuvastatin and ticagrelor.

The persistence of elevated myoglobin levels despite CVVHD, suggested inadequate clearance through standard CRRT therapy. The addition of Cytosorb® represented a rational therapeutic choice, supported by biological evidence, to reduce the toxic burden and mitigate renal injury.

A064

Extracorporeal Hemoadsorption In A Patient With Hypermyoglobinemia Due To Rhabdomyolysis: Our Experience

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Introduction

Rhabdomyolysis is a syndrome characterized by muscle necrosis with the release of creatine kinase and myoglobin into the bloodstream, with a high likelihood of acute tubular renal damage and acute renal failure (1, 2, 3, 4).

Methods

Male, 29 years old, silent medical history. Road accident with multiple compound and exposed fractures in the limbs, surgically stabilized. Left femoral artery severed, surgically reconstructed. In Intensive Care, medical therapy begins with valid respiratory exchanges and hemodynamics supported by norepinephrine (approximately 0.3 mcg/Kg/min) for 12 h.

Progressively increasing hypermyoglobinemia and initiation of hemodialysis treatment with CRRT and extracorporeal hemoadsorption using a Cytosorb filter:

- CVVHDF with heparin for 43 hours;

Qb: 200 ± 5 ml/min, Qd: 5000 ± 200 ml/h, infusion: 2000 ± 300 ml/h, U.F.: 0

Table 1 | Parameters at the admission to ICU and at discharge; comparison between pre/post sorbent myoglobin and CK levels at different timing (0 h, 15 h, 20 h)

	Creat mg/dl	GFR ml/min	K mmol/l	Ca^{++} mmol/l	AST UI/L	albumina g/dl	Hb g/dl	PLT n°	PCR mg/dl	ATIII %	Lattati mmol/l	CK UI/L	mioglob mcg/L
T.I. (IN)	0.55	141	5.2	1.23	172	2.18	6.1	64.000	14.24	69	5.8	**7.263**	**3.421**
T.I. (OUT)	0.78	122	3.4	1.21	84	2.9	8.3	545.000	4.26	130	0.8	**3.421**	**704**

	CK (T 0)	**mioglob** (T 0)	**CK** (T 15 h)	**mioglob** (T 15 h)	**CK** (T 20 h)	**mioglob** (T 20 h)
before-sorbent	5.511	2.922	4.182	2.849	4.532	1.982
after-sorbent	4.585 (-24%)	464 (-84%)	4.108 (-10%)	1.811 (-36%)	4.454 (-1.7%)	1.852 (-6%)

- Citrate CVVHD for 20 hours + extracorporeal hemoadsorption for 20 hours;

Qb: 105 ± 9 ml/min, Qd: 2905 ± 102 ml/h, U.F.: 0

Citrate dose: 3.7 ± 0.2 mmol/l, calcium dose: 1.6 ± 0.1 mmol/l.

Results

On admission to ICU (see Table 1): Blood Pressure: 77/40 mmHg, Mean Arterial Pressure: 50 mmHg. Heart Rate: 147 bpm, SAPS-II: 20, SOFA score: 14. Oligo-anuria with preserved GFR;

At discharge (see Table 1): Blood Pressure: 117/72 mmHg, Mean Arterial Pressure: 87 mmHg, Heart Rate: 95 bpm, Diuresis and GFR preserved.

Conclusions

- There's no definitive agreement in literature about an exact myoglobinemia level for initiating extracorporeal hemoadsorption. In our experience treatment was started at 3,500 ng/ml.
- The comparison between pre/post sorbent myoglobin levels demonstrated excellent efficacy of the treatment in removing myoglobin from the bloodstream, and the sorbent maintained its effectiveness after 18-20 hours.
- The comparison between pre/post sorbent creatine kinase (CK) levels showed a good capacity of the treatment to remove creatine kinase from the bloodstream in the first 12-15 hours.
- Our data suggest that early treatment may better preserve renal function and diuresis, and rapidly stabilize hemodynamics, significantly improving the prognosis.

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A065

Cytosorb Treatment In Septic Patient With Rhabdomyolysis

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Introduction

CytoSorb uses adsorption to enhance hemodialysis, enabling hemoadsorption-hemodialysis (HA-HD) for treating conditions like sepsis, multiple organ failure, liver failure, rhabdomyolysis, and drug overdose. CytoSorb is compatible with all extracorporeal circulation systems, including isolated hemoperfusion, ECMO, CRRT, and cardiopulmonary bypass (CPB).

Methods

64-year-old male with a medical history for chronic alcohol use, smoking, drug abuse, and borderline personality disorder with aggressive and self-harming behavior. He was diagnosed with Crohn's disease and had multiple colonic polyps removed for histological evaluation. He presented to the Emergency Department in a state of confusion, hypothermia, and arterial hypotension. Initial blood tests revealed azotemia (90 mg/dL), elevated creatinine (7.34 mg/dL; baseline: 1.12 mg/dL), markedly increased CPK (17,450 U/L), CK-MB mass (291 ng/mL), and elevated inflammatory markers. A diagnosis of acute kidney injury secondary to rhabdomyolysis in a septic patient was made. Given preserved urine output, treatment was initiated with intravenous hydration, urine alkalinization, and broad-spectrum antibiotics. He was admitted to the Internal Medicine Unit, later transferred to our unit. As his urine output progressively declined and kidney function did not improve, a central venous catheter was placed in the right femoral vein. The patient underwent three hemodialysis sessions, each utilizing 1 CytoSorb, to manage persistent renal impairment and systemic inflammation.

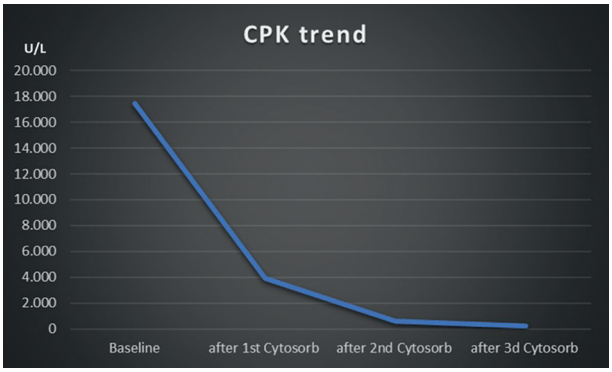

Figure 1 | CPK levels at baseline and after 3 cycles of CytoSorb

Results

At the end of the first session: CPK 3897 U/L, CK-MB mass 9.6 ng/ml; after the second session: CPK 587 U/L, CK-MB mass 1.95 ng/ml; after the third session: CPK 220 U/L, CK-MB mass 2 ng/ml (see figure 1). The patient, having suspended the replacement treatment and removed the CVC, was discharged and, at subsequent follow-ups, a progressive recovery of renal function and resolution of inflammation was evident.

Conclusion

CytoSorb contributed to recovery of renal function and supported the improvement of the patient's septic condition, demonstrating its value as an adjunctive therapy in complex clinical scenarios involving rhabdomyolysis and sepsis.

A066

Hemoadsorption With Cytosorb In Aki Secondary To Rhabdomyolysis Induced By An Experimental Drug For Duchenne Muscular Dystrophy: A Case Report

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Introduction

The accumulation of myoglobin in renal tubules during acute rhabdomyolysis frequently results in acute kidney injury (AKI), often requiring initiation of kidney replacement therapy (KRT). Several studies have demonstrated that the use of the Cytosorb hemoadsorption device can enhance renal recovery in patients with severe rhabdomyolysis.

Methods

We report the case of a 14-year-old male patient with Duchenne muscular dystrophy who developed AKI secondary to rhabdomyolysis, likely associated with the administration of an experimental drug received as part of a clinical trial for Duchenne disease conducted at another institution. Four days after the infusion of the biologic agent, the patient developed vomiting, diarrhea, fever, and gross hematuria. After three additional days, due to reduced urine output and peripheral edema, he presented to the emergency department of our hospital.

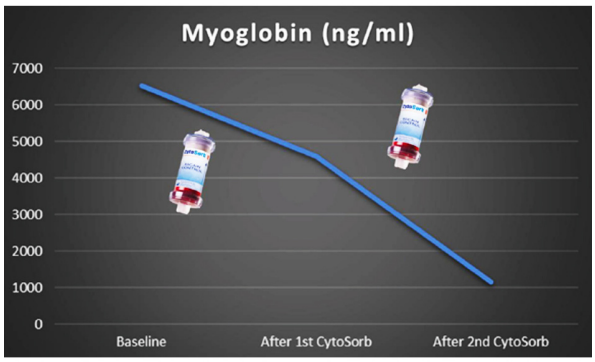

Figure 1 | Myoglobin trend

Initial laboratory findings revealed AKI with a serum creatinine of 1.45 mg/dL and urea of 200 mg/dL, along with anemia, thrombocytopenia, elevated CPK levels (65,590 U/L), and markedly increased serum myoglobin (4,764 ng/mL).

Results

Due to clinical deterioration, the patient underwent two sessions of plasma exchange, multiple red blood cell and platelet transfusions, and three boluses of methylprednisolone (500 mg each). Given the suspicion of atypical hemolytic uremic syndrome (aHUS), treatment with the anti-C5 monoclonal antibody eculizumab was initiated. Simultaneously, intermittent continuous veno-venous hemodiafiltration (CVVHDF) was started (ultrafiltration rate: 30 mL/kg/h; session duration: 8–12 hours), in combination with the Cytosorb adsorbption device.

Following the first treatment session, there was a marked improvement in the patient's clinical condition and a significant reduction in serum myoglobin levels (from 6521 ng/mL to 4601 ng/mL), which further improved after the second treatment (from 4601 ng/mL to 1144 ng/mL) (Fig. 1). CVVHDF sessions were discontinued after normalization of clinical and laboratory parameters. At discharge, renal function and myoglobin levels were within normal limits.

Conclusion

This case supports existing evidence that the use of Cytosorb in conjunction with KRT not only effectively removes circulating myoglobin but may also improve renal and overall clinical outcomes in patients with rhabdomyolysis-induced AKI.

A067

Rhabdomyolysis: A Case Induced By Accidental Overdose Of Rosuvastatin

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Introduction

Rhabdomyolysis is a syndrome characterized by skeletal muscle necrosis with release into the circulation of intracellular contents. The principal cause of rhabdomyolysis are drugs. The diagnostic markers are elevated CPK and serum myoglobin. Statins are the most used drugs for treatment of hypercholesterolemia. Muscle toxicity is an adverse effect rarely associated with renal failure due to rhabdomyolysis.

Methods

We describe the case of a patient admitted to our ICU for renal failure and lactic acidosis in the setting of rhabdomyolysis induced by accidental overdose of rosuvastatin.

History

Patient 73 years old, chronic AF, Diabetes Mellitus on sitagliptin/metformin, hypertension, hypercholesterolemia on **rosuvastatin/ezetimibe**, previous left lateral bulbar ischemic ICTUS.

The patient arrived at the Emergency Department for general malaise associated with diffuse myalgias. Interview with his wife revealed that the patient had mistakenly taken a double dosage of rosuvastatin in the 6 days preceding the onset of symptoms. On admission to our ICU, severe acidosis was found with pH 6.89, lactates 12 mmol/L and anuria. We began hemodialytic treatment with CVVHDF.

Results

On blood chemistry tests CPK 23.541 and MGB not measurable were found. So, there was indication for hemodialytic treatment with Cytosorb. After 24 hours there's a significant reduction of CPK and myoglobin (Table 1).

Table 1 | Hours of hemodialytic treatment with Cytosorb

	CPK presorbent (U/l)	MGB presorbent	CPK postsorbent (U/l)	MGB postsorbent
T = 0	23541	Not measurable	21881	10363
T = 12	18218	17440	17805	17115
T = 24	9311	12255	11758	11536

Conclusion

As shown, hemofiltration with Cytosorb resulted in important reduction of myoglobin and CPK up to 24 hours and especially in the first 6 hours of treatment, still maintaining low values even at 24 hours. Cytosorb, by removing CPK and myoglobin, contributes to the recovery and restoration of renal function and these results can help in improving patient recovery and prognosis.

Drugs Removal

A068

CytoSorb Effect On Quetiapine Intoxication

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Introduction

Quetiapine, lacks a specific antidote in cases of overdose. CRRT may still be considered as part of broader supportive care. In addition to this primary action, CytoSorb has shown potential to adsorb a variety of exogenous substances.

Methods

We report the case of a 30-year-old man, weighing 131 kg with the diagnosis of suspected quetiapine intoxication in an anti-conservative attempt. The patient presents with acute respiratory failure, likely due to central respiratory depression from the overdose, as well as hypoxia and cardiovascular instability, which is being treated with

norepinephrine (NE) to support blood pressure (0.2 mcg/kg/min). The patient developed gastroparesis and paralytic ileus secondary to anticholinergic effects from the drug overdose. The high plasma quetiapine concentration of 7,920 ng/ml (normal range: 40–400 ng/ml) confirms a significant overdose, which underscores the need for aggressive intervention. CRRT (Continuous Renal Replacement Therapy), specifically CVVHDF, is initiated due to the high plasma concentration of quetiapine. The addition of CytoSorb aims to enhance the removal of exogenous substances like quetiapine. CRRT + CytoSorb is continued for 48 hours, with cartridge changes every 24 hours, which is a key factor in ensuring efficient drug clearance.

Results

After 48 hours of treatment, the plasma concentration of quetiapine drops to 392 ng/ml, within the normal range. This reduction in drug concentration suggests that the combined CRRT + CytoSorb therapy was effective in removing quetiapine from the bloodstream. The norepinephrine (NE) support is gradually tapered and eventually discontinued on the second day after the end of CRRT + CytoSorb (see figure 1).

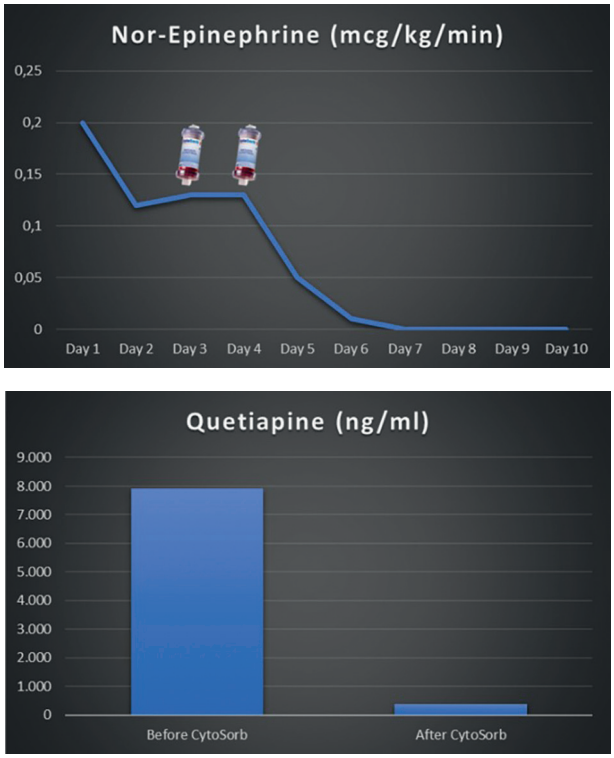

Figure 1 | Norepinephrine trend and quetiapine values during treatment with CytoSorb

Conclusion

CytoSorb appears to have been beneficial in rapidly reducing the plasma concentration of quetiapine. Considering that Quetiapine overdose lacks a specific antidote, and potential co-ingestion of other drugs necessitates comprehensive supportive care, including airway management and cardiovascular monitoring. Physostigmine may be used cautiously under ECG monitoring but is contraindicated with conduction issues. Gastric lavage may help selectively. Quetiapine's elimination half-life is approximately 12 hours.

A069

Acute Intoxication With Quetiapine Treated With CytoSorb: A Case Report

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Introduction

While many drug poisonings are successfully treated with specific antidotes, tricyclic antidepressant and/or atypical neuroleptic intoxications still represent a major challenge. In addition to conventional approaches, a novel hemadsorption device could represent a therapeutic opportunity for detoxification.

Methods

Here we report the case of an 18-year-old female with borderline personality disorder admitted for anticonservative use of Flurazepam, Fluoxamine, Risperidone, Quetiapine, and Alprazolam. The patient was in coma (GCS 3), spontaneuslybreathing with blood gas analysis in metabolic acidosis and modest increase in serum lactates. The patient was hypotensive in sinus tachycardia in complete LBBB. Sedation, orotracheal intubation and

controlled ventilation, hydration with crystalloids and correction of metabolic acidosis were then performed, with complete regression of LBBB and persistence of RBBB on ECG. Given the persistence of hypotension, continuous infusion of low-dose norepinephrine was started.

Blood tests showed: Quetiapine 19.1710 ng/ml (active metabolite: norquetiapine21489 ng/ml), Risperidone 132 ng/ml, Flurazepam 235 ng/ml, Fluoxamine72 ng/ml, Alprazolam 45.55 ng/ml, Creatinine 1,10 mg/dl, Azotemia 41 mg/dl , electrolytes in range, CPK 4185 U/l, normal liver function.

At an initial nephrological consultation, dialysis therapy alone was not considered sufficient to remove the molecules in question. Subsequently, given the CK value > 4000 U/l, accompanied by a serum concentration of quetiapine of approximately 20,000 ng/ml (the toxic dose is considered greater than 400 ng/ml), CVVDHF was started with Cytosorb for 3 cycles (1 cartridge every 24 hours in post-filter).

Results

After CVVHDF with 3 cycles of Cytosorb, given the reduction in the dosage of noradrenaline and the blood dosages of Quetiapine (2200 → 2336 → 1695 ng/ml), dialysis therapy and the sorbent were interrupted (Fig.1).

Progressive recovery of consciousness and subsequent extubationon 4°day.

The patient was transferred to CSM on day 10.

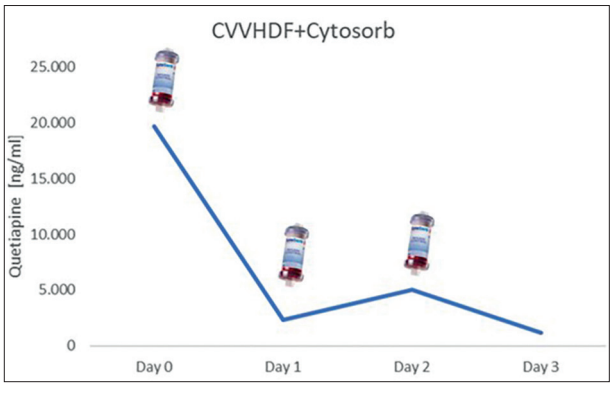

Figure 1 | Plasma levels of quetiapine during continuous venous haemodiafiltration (CVVHDF) + 3 haemadsorption treatments in 3 days

Conclusion

In the absence of a proven beneficial therapeutic regimen and specific antidotes, the use of CytoSorb represents an alternative treatment for life-threatening complications of quetiapine intoxication. In particular, the efficacy of this adsorption technique for intoxications caused by lipophilic agents should always be evaluated, given the impossibility of CVVHDF alone to remove them.

A070

Use Of Cytosorb For The Resolution Of A Severe Simultaneous Intoxication Case Of Apixaban And Digoxin

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Introduction

Digoxin is a drug used for heart failure and arrhythmias and Apixaban is an anticoagulant used for atrial fibrillation.

Both substances are normally eliminated by the kidneys, but they cannot be removed by standard dialysis as they are hydrophobic compounds bound to proteins.

CytoSorb® is useful in cases of drug intoxications involving hydrophobic molecules to remove excess substances while simultaneously treating some secondary complications, such as liver failure, hyperinflammation, or rhabdomyolysis.

Methods

A patient with type II diabetes, chronic kidney disease, atrial fibrillation, and cognitive impairment was hospitalized for vomiting and diarrhea. During the episode,

the patient continued taking Metformin, Apixaban, and Digoxin, developing MALA, AKI, and hyperkalemia, in addition to severe digoxin intoxication (3.4 ng/mL) and Apixaban overdose (106 ng/mL).

Due to the persistence of oliguria and lactic acidosis, hemodialysis was attempted but failed due to hemodynamic instability. SLED with CytoSorb® (8 hours) was then chosen.

Results

The use of CytoSorb allowed a reduction in Apixaban (-46.8%) and digoxin (-25%) without albumin loss.

The patient showed improvement in hemodynamics and ECG, with resolution of the junctional rhythm.

The recovery of diuresis allowed the definitive suspension of dialysis the following day after the end of Cytosorb treatment.

Conclusion

The treatment with CytoSorb® showed effectiveness as early as the first 4 hours, with a rapid reduction in serum levels of Apixaban and Digoxin (46.7% and 16.6% reduction from baseline, respectively), while a steady state was reached in the last 4 hours (Figure 1-A).

A reduction in Interleukin-6 (IL-6) and free light chains (FLC) K and λ levels was also observed, particularly in the first 2 hours of treatment (Figure 1-B).

These results suggest that CytoSorb® is effective when combined with SLED in patients who do not require intensive care.

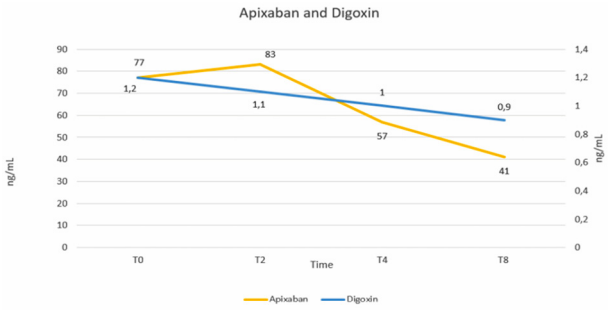
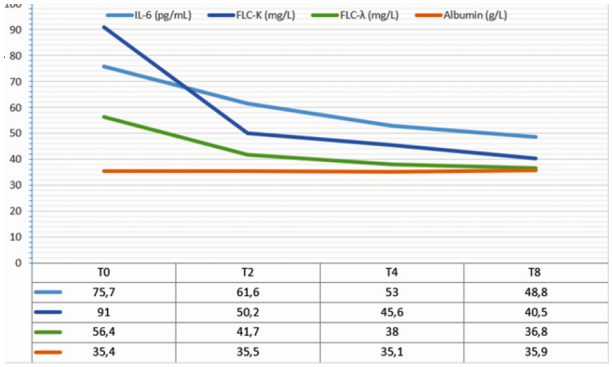


Figure 1-A | Reduction in serum levels of Apixaban and Digoxin in 8 hours



	T0	T2	T4	T8
IL-6 (pg/mL)	75,7	61,6	53	48,8
FLC-K (mg/L)	91	50,2	45,6	40,5
FLC-λ (mg/L)	56,4	41,7	38	36,8
Albumin (g/L)	35,4	35,5	35,1	35,9

Figure 1-B | Il-6, FLC-K, FLC- λ, Albumin concentrations

A071

Hemoperfusion With CytoSorb In A Case Of Valproic Acid Poisoning

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Introduction

The use of the CytoSorb adsorber in any extracorporeal circulation allows the removal of various types of potentially toxic and/or harmful molecules from the bloodstream.

In addition to endogenous molecules produced by the body, CytoSorb is also capable of removing several drugs. For certain classes of drugs, such as antiepileptics, only in vitro data are currently available.

Methods

Clinical case of a 57-year-old female patient admitted to the Intensive Care Unit due to intentional intoxication with Valproic Acid (VPA) and bisoprolol.

Upon admission to the ICU, the patient presented with a Glasgow Coma Scale (GCS) score of 8, mean arterial pressure (MAP) of 50 mmHg, Heart Rate of 38 bpm, VPA blood level of 440 µg/mL (normal range 50–100 µg/mL), severe metabolic acidosis (pH 7.1, HCO3- 9, base excess -15, lactate 6.5). Aminergic support and non-invasive ventilation (NIV) in BiPAP mode were initiated. In light of the clinical and laboratory findings, a combined treatment approach was decided: isolated hemoperfusion (HP) with CytoSorb combined with extracorporeal therapy in continuous veno-venous hemofiltration (CVVH) mode.

Two CytoSorb cartridges were used sequentially, with the first cartridge replaced after the initial 12 hours of treatment, for a total of 24 hours of hemoperfusion therapy.

Results

At the end of the first 12 hours, the VPA blood level was 100 µg/mL, while after 24 hours of treatment, the patient's VPA blood level was 55 µg/mL (Figure 1). The metabolic abnormalities were fully corrected (pH 7.38, HCO3- 25, base excess 1.1, lactate 0.9), MAP was 100 mmHg, HR was 74 bpm, aminergic support was completely discontinued, and the patient was breathing spontaneously.

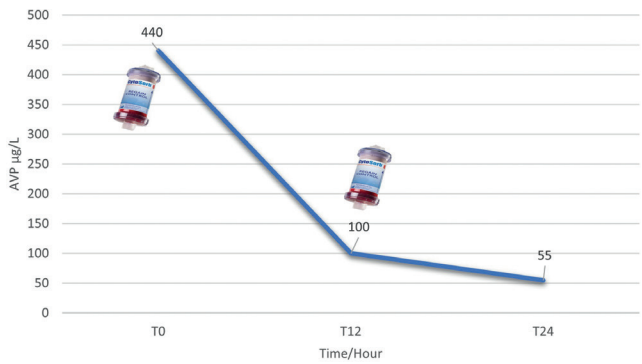

Figure 1 | VPA blood levels over 24 hours

Conclusions

Hemoperfusion with CytoSorb proved to be an effective and safe method for the in vivo removal of Valproic Acid, enabling the rapid resolution of a case of severe polypharmacologic intoxication.

A072

Pharmacokinetic Of Cefiderocol During CRRT And CytoSorb Therapy

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Introduction

Cefiderocol is a new broad-spectrum cephalosporine antibiotic with promising activity against Gram-negative bacteria, including carbapenem-resistant strains. PK/PD analyses on the use of Cefiderocol in critically ill patients subjected to extracorporeal procedures are still limited. The pharmacokinetic and pharmacodynamic (PK/PD) properties of Cefiderocol have been evaluated during CRRT and Cytosorb.

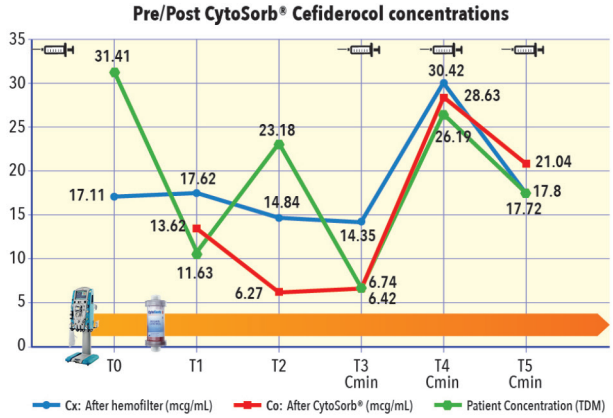
Methods

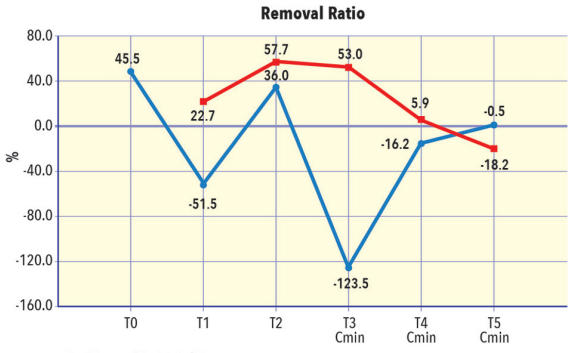
A 16-year-old male was admitted to the Pediatric Intensive Care Unit (PICU) following acute respiratory failure caused by adenovirus pneumonia, and acute obstructive renal failure as consequence of hemorrhagic cystitis. Patient was treated off-label with Cefiderocol 2 g every 8 hours for suspected septic shock in the context of severe immunodeficiency. Antibiotic was administered intrave-

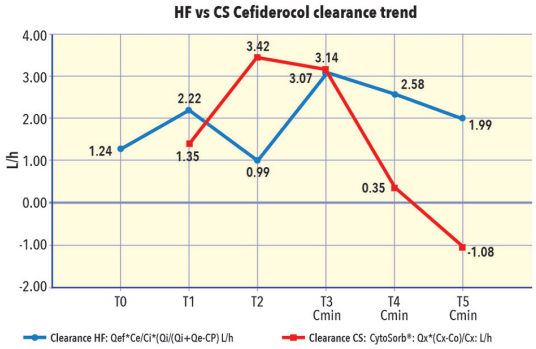
nously with an infusion over three hours. Blood samples were taken immediately before the start of HA (T0), and then at 1 hour (T1), 3 hours (T2), 5 hours (T3-Cmin), 16 hours (T4-Cmin), and 24 hours (T5-Cmin).

Results

Regarding the contribution of hemofilter clearance (CLHF) we observed a maximum CLHF at T 3 (3.07 L/h) and a minimum CLHF at T 2 (0.99 L/h) (Figure 1). We have calculated Cytosorb removal rates (RR%) at the different time points: 23% (T 1), 58% (T 2), 53% (T 3), 6% (T 4), 18% (T 5). Hemofilter removal rates (RR%) 45% (T 0), 34% (T 1), 36% (T 2), 55% (T 3), 14% (T 4), 3% (T 5). The overall mass removal for Cytosorb ® was -590 mcg/hour and for the Hemofilter -95 mcg/hour (Figure 1).







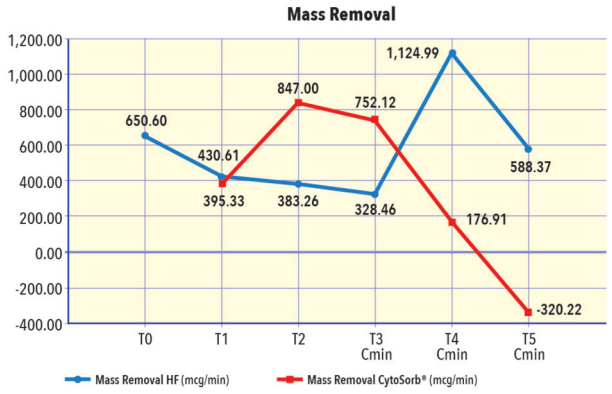


Figure 1 | Upper and left section: Time course of the antibiotic unbound concentrations (patient green line), (posthemofilterbluline), (post-cartridge red-line). Upper and right section: Time course of the hemofilter and cartridges' removal ratio at the different time points. Lower and right section: Time course of the hemofilter and cartridges' clearance at the different time points. Lower and left section: Time course of the hemofilter and cartridges' mass removal at the different time points

Conclusion

Based on the results described here, we could suggest that a supplementary dose of cefiderocol should be administered during the first 120 minutes of hemoadsorption with Cytosorb®. The pharmacokinetic behavior of cefiderocol during CRRT suggests that cefiderocol infusions could be prolonged over a longer duration (2-3 hours) with every 6 hours instead of 8hours interval.

A073

Hemadsorption Therapy In Severe Psychotropic Drug Overdose: A Case Report

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Introduction

Hemadsorption devices like CytoSorb® are increasingly utilized in critical care for drug intoxication, particularly when antidotes are unavailable or ineffective. This technique facilitates rapid drug removal, improving patient outcomes in severe overdose cases.

Methods

A 23-year-old man with a history of personality disorder and previous drug abuse was admitted to the emergency department in an altered state of consciousness after ingesting multiple psychotropic medications. He consumed approximately 60 tablets of Quetiapine 50 mg (3000 mg total), 28 tablets of Clozapine 100 mg (2800 mg total), 25 tablets of Paroxetine 20 mg (500 mg total), 10 tablets of Delorazepam 0.5 mg (5 mg total), and 10 tablets of Alprazolam 1 mg (10 mg total). Upon arrival, he had a Glasgow Coma Scale score of 8, peripheral oxygen saturation 80% on room air, normal blood pressure, sinus tachycardia, and a QTc interval of 494 ms.

Mechanical ventilation was initiated. Esophagogastroduodenoscopy revealed numerous ingested tablets, including 30 quetiapine tablets and various fragments, which were removed. The patient was transferred to the ICU and treated with CVVHDF connected to a CytoSorb® cartridge to accelerate drug removal from the bloodstream.

Blood samples were collected before and after 24 hours of hemoadsorption.

Due to low baseline concentrations of some drugs, only paroxetine, alprazolam, clozapine and norclozapine levels were measured.

An informed consent was obtained from the patient for publication of this case report.

Results

The baseline and the 24-hour drugs concentrations are shown in *Fig. 1*.

Hemadsorption continued additionally for 24 hours with two cartridges over 48 hours.

Following hemadsorption, the patient regained consciousness, became cooperative, and was extubated on day two. By day five, patient was transferred to the psychiatric ward.

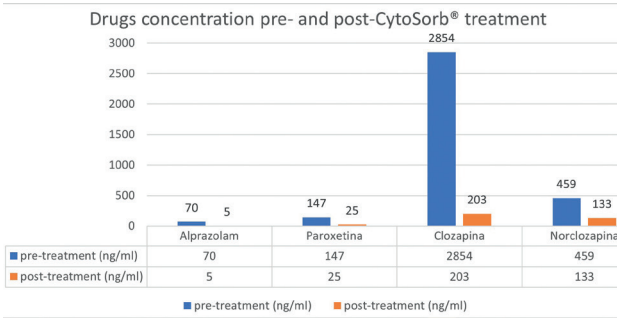

Figure 1 | Drugs levels during hemadsorption treatment

Conclusion

Hemadsorption with CytoSorb® was safe, feasible, and effective in removing multiple psychotropic drugs in this case of severe overdose.

A074

Adsorption In The Management Of DOAC Intoxications, A New Perspective

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Introduction

Poisoning from oral direct-acting anticoagulants (DOAC) is a fearful event, since the antidote is not always immediately available. The same goes for digoxin. However, the advent of sorbent cartridges in this field, such as Cytosorb, has allowed us to obtain excellent results in the management of these patients. Below we report our experience with a clinical case.

AKI And Digoxin Intoxication: Hemodialysis Treatment With Sorbent

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Introduction

Digoxin intoxication is a life-threatening condition that causes possible serious arrhythmias and requires life-saving treatment. The main therapeutic option is a specific antidote that is not always available. In case of AKI with hyperkalemia due to digitals intoxication, emergency treatment with haemodialysis-haemoperfusion using sorbent can be indicated.

Methods

An 84 years old woman joined the ED for severe bradycardia with HR 22-25 bpm, BP 100/50 mmHg. In medical history CAF in DOAC, episodes of acute heart failure, DM II NID, CKD- eGFR -EPI 52 ml/min, lab tests: creatinine 5.3 mg/dl, K+ 8.9 mmol/L, digoxin 3.7 ng/ml (n.v. 0.8-2), unbalanced metabolic acidosis and hyperlactacidemia (lactate 10.6 mmol/L), tachypneic, noslopping aedema, anuria diagnosis: AKI in digoxin intoxication, hyperkalemia, hemodynamic instability. Renal ultrasound: kidneys within normal limits in consideration of the clinical presentation, urgent hemodialysis treatment is indicated. Placement of CRRT and Cytosorb, systemic anticoagulation with UFH.

Discussion

Due to the unavailability of the antidote, hemodialysis treatment with sorbent cartridge was performed. After 4 hours of CRRT reduction in digoxin blood level (2 ng/ml), improvement in kaliemia control (K+ 4.8 mEq/L), reduction in hyperlactacidemia (lactate 6.5 mmol/L), BNP drop were observed. During treatment HR 210 bpm occurred, and then adenosine bolus was given with normalization of HR. After 17-hours CRRT treatment, two additional

Methods

We present here a case of a female patient aged 84, with a history of ischemic-hypertensive heart disease complicated by dilated cardiomyopathy with reduced ejection fraction (35%) and episodes of Paroxysmal Atrial Fibrillation, Chronic Kidney Disease stage G4 KDIGO 2012. In pharmacological history Digoxin 0.25 mg/day, Apixaban 15 mg one tablet/day. She arrives in the emergency area for dyspnea and general malaise. Blood tests: Azotemia: 170 mg/dl, Cr/P: 3.6 mg/dl, Potassium: 5.2 mmol/l, INR: 5, APTT: 50 s, Digoxinemia: 3.2 pg/ml. At the E.O. general patient tachypneic, rhythmic cardiac activity with severe bradycardia (40 BPM). Patient with type 1 cardio-renal syndrome with probable DOAC and Digitalis intoxication.

Results

In consideration of the reduced clearance of Digoxin and Apixaban with standard hemodialysis techniques, after positioning of right femoral CVC, we scheduled 24-hour CVVH with Seleparin in continuous infusion (10 IU/h) for 24 hours, Uf: 100 ml/h in association with hemoperfusion with Cytosorb sorbent. After a treatment cycle, we see improvement of clinical parameters, Digoxinemia: 1.7 pg/ml, disappearance of electrocardiographic signs of digitalis impregnation, HR: 60 bpm. Also improved coagulation status with INR: 2.8, APTT: 40s.

Conclusion

Adsorption by means of sorbent cartridges is increasingly present in the panorama of extracorporeal replacement techniques. In particular, Cytosorb, in consideration of its structural characteristics and the degree of porosity, surface and geometry of the polystyrene resin, is a new alternative in the conditions of intoxication and poisoning not responsive to medical therapy. This is particularly true in patients in critical conditions, managing to remove high molecular weight molecules, such as fungal toxins (Aflatoxin from Amanita Phalloides) or drugs for which antidotes are not available in the territory (antibody directed towards the fractions of digoxin and Andexanet Alfa for DOACs directed against activated factor X).

PARAMETERS	AT ADMISSION	AFTER 17 HOURS
Glasgow coma scale (GCS)	13	15
Heart rate (bpm)	29	80
Blood pressure (mmHg)	100/50	116/60
Serum digoxin (ng/ml)	3.7	1.6
eGFR (CKD-EPI ml/min/1.73m$_2$)	7	21
K+ (mmol/L)	8.9	4.4
Serum lactate (mmol/L)	10.6	1.3
pH	7.37	7.46
Sodium Bicarbonate (mmol/L)	21	25
WBC(mila/microL)	12.3	6.5
CRP (mg/L)	0.34	1.2

Figure 1 | Several parameters at admission and after 17 hours

intermittent haemodialysis sessions were required due to the persistence of anuria. Hospitalization was complicated by UTI: urine culture + E. coli. The patient was discharged after 20 days with renal function recovered – creatinine 1.4 mg/dl, K+ 4.1 mmol/L.

Conclusions

Hemodialysis treatment with sorbent in digoxin toxicity is effective in terms of blood level reduction; length of treatment remains to be debated. We observed an improvement in serum digoxin level after 4 hours and normalization after 17 hours of hemodialysis treatment (Fig.1). The effectiveness of treatment might depend on the initial blood levels of digoxin.

A076

Hemoperfusion With Cytosorb In Acute Pediatric Carbamazepine Intoxication: A Case Report

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Introduction

Carbamazepine (CBZ) intoxication is a potentially life-threatening condition due to its narrow therapeutic index and slow metabolism. In severe cases with central nervous system depression, extracorporeal removal may be considered. We report the case of a 7-year-old girl treated with Cytosorb® hemoperfusion following acute CBZ overdose.

Methods

A 7-year-old female patient, with a body weight 22 kg, and a known history of focal epilepsy (on chronic CBZ therapy), autism spectrum disorder, and intellectual disability presented with coma (GCS 3/15) after suspected ingestion of 4000 mg of CBZ (57 mg/kg). Initial serum CBZ level was 144 µmol/L. Following intubation and gastric decontamination (activated charcoal, intralipid, and EGDS), a short term hemodialysis central venous catheter was placed and a Cytosorb hemoperfusion cycle was initiated, along with low-dose norepinephrine and continuous heparin infusion titrated to ACT values. The patient was sedated and invasively ventilated during the procedure.

Results

Hemoperfusion was performed over a 8 hours period (Qb 150ml/min) and was well tolerated, with stable hemodynamics and no adverse events. A rapid decline in CBZ levels was observed (144 → 139→ 39 → 29 → 10 µmol/L over 48 hours) (figure 1). The patient regained

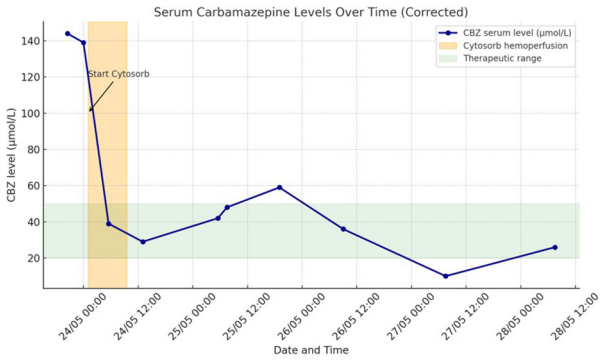

Figure 1 | Serum Carbamazepine levels over time

consciousness progressively and was successfully extubated on day 3. EEG and cardiac evaluations were normal. She was transferred to the Neurology Unit in stable condition, with full neurological recovery (GCS 15/15) and resumption of enteral feeding. CBZ was gradually reintroduced at a lower dose before discharge.

Conclusion

This case highlights the potential role of Cytosorb hemoperfusion in managing severe CBZ intoxication in pediatric patients. Despite CBZ's high protein binding, early extracorporeal removal in combination with standard detoxification measures was associated with rapid clinical improvement and normalization of serum levels. Further studies are needed to confirm the efficacy and safety of Cytosorb in pediatric toxicology.

A077

Use Of The CytoSorb® In Drug And Toxins Poisoning: A Narrative Review

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Introduction

Acute poisoning due to drugs or exogenous toxins is a potentially life-threatening clinical condition, often characterized by metabolic shock, multiorgan failure, and lactic acidosis. In the most severe cases, extracorporeal detoxification may be essential to ensure patient survival and prevent irreversible organ damage. CytoSorb®, thanks to its high surface and biocompatible polymer beads, enables the removal of hydrophobic molecules with a molecular weight of up to 55 kDa, including cytokines, bilirubin, myoglobin, ticagrelor, rivaroxaban, drugs and toxic pharmacological substances. Its use in the field of toxicology is emerging as an effective adjunct to conventional intensive care therapies, particularly in patients with limited therapeutic alternatives.

Methods

We reviewed five clinical cases treated between 2019 and 2024 for acute poisoning: three cases of metformin overdose, one of quetiapine overdose, and one case of toxic mushroom ingestion (*Clitocybe dealbata*). All patients presented with acute kidney injury (AKI), severe metabolic acidosis (pH < 7.0, lactate > 9 mmol/L), shock requiring vasopressor support, and a poor prognosis (APACHE IV scores ranging from 48 to 100). Continuous veno-venous hemodialysis (CVVHD) combined with CytoSorb therapy was initiated in all cases, for durations ranging from 24 to 72 hours. Treatment was supplemented with supportive therapy including antibiotics, vasopressors, bicarbonate infusions, and, in selected cases, intravenous immunoglobulins or activated charcoal.

Results

All patients demonstrated resolution of lactic acidosis, recovery of spontaneous diuresis, and hemodynamic stabilization with withdrawal of vasopressor support. In the metformin cases, CytoSorb contributed to rapid detoxification despite the presence of septic shock and severe renal dysfunction. The quetiapine case resulted in progressive neurological and cardiac recovery. In the case of mushroom poisoning, hemoadsorption facilitated renal function recovery and metabolic rebalancing.

Conclusion

CytoSorb therapy represents an effective and safe adjunctive option in the management of complex acute poisonings, particularly in the setting of shock and multiorgan failure. Its ability to remove toxins, drugs and cytokines may significantly improve clinical outcomes in critically ill patients. These documented clinical experiences support the early integration of CytoSorb into intensive care management strategies for severe intoxications.

Cardio

A078

A Light In The Dark: Pancreatic Stone Protein Doesn't Seem To Be Affected By Immunosuppressive Induction Therapy In Cardio-Surgery Patients

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Introduction

Pancreatic stone protein (PSP) is indeed emerging as a promising biomarker for diagnosing infections, particularly in critically ill patients. Research has demonstrated that PSP levels can rise in response to infections especially in settings such as intensive care units (ICUs). The aim of this experimental study was to evaluate the role and potential of PSP as a marker of sepsis in heart transplant recipients and cardiac surgery patients by comparing it with traditional inflammation markers.

Methods

A total of 33 patients were enrolled, of whom 6 underwent heart transplantation (TRAP group) and 27 underwent cardiac surgery (NTRP group). Patient data were collected according to the following Timeline: Preoperative data; During surgery; On the first postoperative day; Every three days thereafter (fourth, seventh, tenth day); At delivery.

Results

In our center, the immunosuppressive protocol includes induction with anti-thymocyte globulins in all recipients. A significant increase in PCT in the post-operative period has been observed related to thymoglobulin therapy and not related to ongoing infection. It is also known that the diagnostic accuracy of PCT is lower in immunosuppressed and neutropenic patients. If, however, PSP were to prove, as it seems, a biomarker not influenced by immunosuppressive therapy (there are no differences in trend in the TRAP and NTRP groups), it could represent a good weapon in the early detection of sepsis in transplant patients. The leukocyte count is unreliable in transplant patients in terms of early detection of sepsis, since it is a value "dirtied" by immunosuppressive therapy, (Fig. 1).

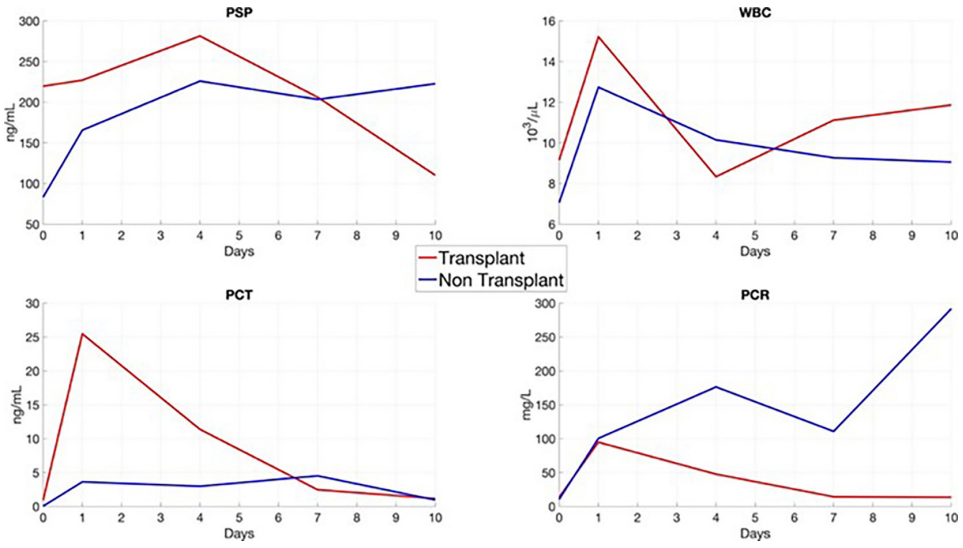

Figure 1 | Trend of sepsis biomarker in critically ill patient submitted to cardiac surgery (Transplant and not transplant)

Conclusion

Traditional inflammation indices (PCT, PCR, WBC) are altered by immunosuppressive induction therapy, making them deficient in terms of their interpretation in terms of early detection of infection. PSP, having a comparable trend between the TRAP and NTRP groups, does not seem to be affected by this influence.

A079

Successful Employment Of VA ECMO And Blood Purification In Cardiogenic/Septic Shock: A 2 Cases Series

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Introduction

Sepsis in patients with a reduced cardio-circulatory reserve may precipitate a particular phenotype of shock, marked as cardiogenic/septic shock, characterized by systemic pressure collapse, sharp lactate increments, and deep central venous desaturation. VA ECMO and blood purification could be potentially life-saving in such a clinical scenery.

Methods

Two male patients, 59 and 75 years old, with a reduced LVEF due to ischemic heart disease, underwent surgical cardiac revascularization. The emergence of a sepsis complicated the postoperative course, causing an arterial hypotension unresponsive to cathecolamines and a microcirculatory failure, in spite of a normal cardiac index (CI). In front of a DO_2-dependant cardiogenic/septic shock, in both cases, a peripheral VA-ECMO was established to increase CI and oxygen availability (DO2I), while a CVVHDF was started to replace renal function. A CytoSorb cartridge was used in both cases to prevent end-organ damage mediated by cytokine, and restore peripheral vasomotor responsiveness. In one patient an eight hours run with oxYris, a filter able to absorb the endotoxin, was delivered before CytoSorb implementation. An IABP was also inserted to ensure a LV unloading and an empirical antibiotic therapy was commenced. In both cases blood culture became positive to Gram+ agents.

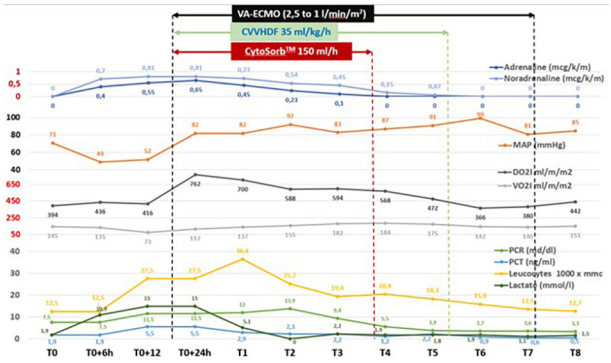

Figure 1 | Patient A

Results

The prompt institution of a VA-ECMO increased the CO, restored the oxyphoric indices, and, together with cytokine hemoadsorption, stabilized the MAP, promoted a fast clearance of serum lactates and a fast weaning from cathecolamine, and ensured end-organs protection, (Fig 1).

Conclusions

In literature, the patients with LV dysfunction and sepsis who died had a significantly lower ScvO2 than survivors: therefore, management strategies targeting DO2 variables (such as VA-ECMO) may be strongly indicated to treat the threatening dysoxia. The combined use of VA-ECMO and blood purification therapies demonstrated potential benefit as a bridge to recovery in cardiogenic/septic shock.

A080

Pancreatic Stone Protein (PSP) Correlates With The Clinical Severity Of Patients Underwent Heart Transplantation And Cardiac Surgery

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Introduction

Given the critical nature of heart transplant recipients and cardiac surgery patients, early and accurate detection of sepsis is crucial for improving outcomes. Since traditional inflammation markers like C-reactive protein (CRP) and procalcitonin (PCT) are commonly used but may have limitations in specificity or sensitivity, assessing PSP as a potential biomarker for sepsis is especially relevant.

Methods

A total of 33 patients were enrolled, of whom 6 underwent heart transplantation (TRAP group) and 27 underwent cardiac surgery (NTRP group). Patient data were collected according to the following Timeline: Preoperative data; During surgery; On the first postoperative day; Every three days thereafter (fourth, seventh, tenth day); At delivery.

Results

Figure 1 shows in the TRAP group a positive correlation (r=0.7) statistically significant (p=0.0005) between the PSP and the SOFA values, so it can be reasonably assumed that an increase in the PSP corresponds to an increase in the SOFA score. In the NTRP group this correlation remains positive and statistically significant, maintaining the same statements made in transplant recipients. The

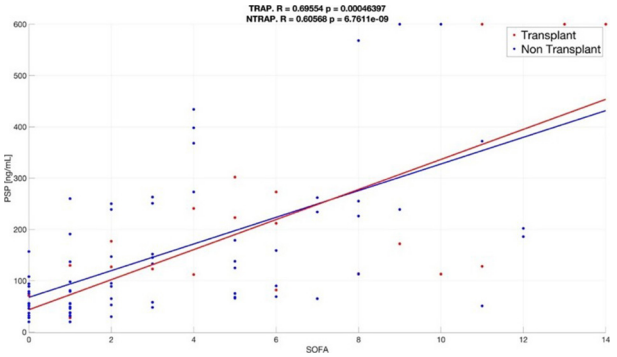

Figure 1 | Correlation between the PSP and the SOFA values in patients underwent heart transplantation and cardiac surgery

threshold in our population is 91 ng/mL, which means starting from a PSP level greater than or equal to 92 ng/mL, in our population it is more likely to have a patient who develops sepsis later. The AUC is 0.73. This difference between the cut-offs usually observed (approximately equal to 200 ng/ml) and the one we identified could be explained by the complexity of cardiac surgery.

Conclusion

Pancreatic Stone Protein (PSP) can be defined as a promising early marker of sepsis whose dosage is made easily accessible by the AbioSCOPE Point of Care measurement method. Given that SOFA is one of the most widely used scores to monitor the progress of the disease, this can lead us to intuit that PSP correlates with the clinical severity of the patient.

A081

Efficacy Of Hemoadsorption Therapy In The Treatment Of Post-surgical Hyperbilirubinemia Due To Aortic Dissection: A Case Report

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Background

Aortic dissection represents a complex surgical condition, often associated with high morbidity and multiorgan complications in the postoperative period, such as ischemic liver injury due to hypoperfusion. This ischemic injury directly results in a hepatic overproduction of bilirubin. Timely implementation of extracorporeal support therapies, such as CRRT combined with Cytosorb -the only certified adsorbent cartridge for the removal from whole blood of bilirubin, cytokines, myoglobin, ticagrelor, and rivaroxaban- can lead to a marked improvement in clinical parameters.

Case Description

The patient underwent surgical intervention for aortic dissection. The initial clinical presentation was characterized by preoperative cardiac tamponade and biventricular systolic dysfunction, which required intensive inotropic support. In the postoperative course, there was a marked elevation of hepatic enzymes, with total bilirubin peaking at 19.7 mg/dL and direct bilirubin at 16.0 mg/dL, suggesting ischemic liver damage due to hypoperfusion resulting from hemodynamic compromise. Confronted with hyperbilirubinemia, the patient was treated with CRRT and Cytosorb (administered for 48 hours using two cartridges) with the aim of rapidly reducing bilirubin levels and controlling the inflammatory response.

Laboratory evaluations showed a progressive normalization of hepatic parameters, with a decrease in both total and direct bilirubin levels, accompanied by an overall clinical improvement (Fig.1).

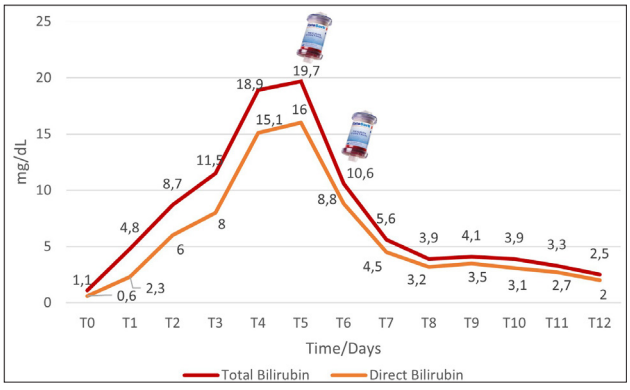

Figure 1 | Total and Direct Bilirubin trend

This improvement is evident from other liver function parameters (compared pre- and post-treatment), such as AST decreasing from 59 U/L to 20 U/L, CPK decreasing from 334 U/L to 71 U/L, and LDH decreasing from 1004 U/L to 366 U/L.

The prompt therapeutic intervention allowed the normalization of laboratory values, gradual weaning from CRRT, and the patient's discharge.

Conclusions

The use of Cytosorb enabled the containment of the systemic inflammatory response and the mitigation of postoperative ischemic liver injury, thereby facilitating the recovery of hepatic function. Cytosorb proved effective in reducing elevated bilirubin levels, improving liver function, and stabilizing hemodynamic status.

A082

Cytosorb Hemoadsorption For Dabigatran Removal In Emergency Mitral Valve Surgery: A Case Report

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Introduction

Dabigatran, a direct thrombin inhibitor, is commonly used for stroke prevention in patients with atrial fibrillation. However, its anticoagulant effects pose a significant challenge in emergency cardiac surgery, where rapid reversal is crucial to minimize perioperative bleeding risks. While Idarucizumab is a specific reversal agent for Dabigatran, extracorporeal removal techniques, such as Cytosorb hemoadsorption, have gained attention

as effective alternatives, especially in cases requiring cardiopulmonary bypass (CPB). Cytosorb has demonstrated efficacy in reducing circulating Dabigatran levels, enhancing haemostatic management in critical surgical settings.

Methods
An 80-year-old female patient with a history of atrial fibrillation on chronic Dabigatran therapy presented with worsening dyspnea and congestive heart failure due to severe mitral regurgitation. Following initial medical stabilization, she was scheduled for urgent mitral valve repair. Given her recent intake of dabigatran and the associated haemorrhagic risk, Cytosorb hemoadsorption was integrated into CPB to facilitate anticoagulant removal and optimize perioperative haemostasis.

Preoperative laboratory tests revealed a dabigatran level of 74 ng/mL, with an activated partial thromboplastin time (aPTT) of 43 seconds and an international normalized ratio (INR) of 1.48. Intraoperatively, the patient underwent CPB for 77 minutes with an aortic cross-clamp time of 45 minutes.

Results
Cytosorb was positioned in the extracorporeal circuit in a post-pump configuration, allowing continuous hemoadsorption throughout CPB. Postoperatively, Dabigatran levels were significantly reduced, with a measured post-CPB level of 12.3 ng/mL, accompanied by an INR of 1.80 and an aPTT of 80 seconds, without excessive bleeding or hemodynamic instability. Quantra analysis showed a pre-CPB clot stiffness of 188 and a post-CPB value of 185, indicating maintained coagulation integrity. The patient remained stable in the intensive care unit, with progressive normalization of coagulation parameters and a total blood loss of 750 ml.

Conclusion
This case highlights the successful use of Cytosorb hemoadsorption for Dabigatran removal in an emergency mitral valve repair setting. Cytosorb effectively reduced anticoagulant levels, mitigating perioperative bleeding risks and allowing for safe surgical intervention. These findings support the role of extracorporeal hemoadsorption as a valuable tool in managing patients on direct oral anticoagulants requiring urgent cardiac surgery.

A083

Emergency Cardiac Operations In Patients At High Risk Of Bleeding – A Single Centre Experience

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Introduction
Open heart operations are always at high risk of bleeding due to treatment with coagulation-active substances. Patients requiring coronary artery bypass grafting (CABG) are often loaded with antithrombotic drugs (AT) and have an increased risk of perioperative bleeding complications. Active AT removal by hemoadsorption (CytoSorb®) integrated in the cardiopulmonary bypass circuit (CPB) is increasingly used in this setting to reduce bleeding. The aim of our study is to analyse the impact of CytoSorb® and evaluate the results.

Methods
We investigated 55 consecutive patients who underwent emergency cardiac surgery for CABG at our institution between January 2023 and January 2025. 14 patients were receiving Ticagrelor (n = 10) or Rivaroxaban (n = 4). AT were discontinued one day before surgery in nine patients and on the day of surgery in one patient. In 7 cases we installed CytoSorb® into CPB. Bleeding complications and drainage volumes during and after surgery were analysed in detail, and compared with 7 patients without adsorption.

Results
In the CytoSorb® group no re-thoracotomies had to be performed. Drainage volumes in 24 hours were 300 mL (IQ: 300-450 mL) 350 mL (IQ: 280-400 mL) for patients on Ticagrelor and Rivaroxaban, respectively. Mean operation time was 184 ± 35 min. One patient had a minor

bleeding event and there were no surgical re-explorations for bleeding. In most of patients, transfusions of blood products were not needed. Compared with control group, multiple bleeding complications occurred. These were associated with longer total operation time (p = 0.0040), higher drainage volumes (p = 0.0037), more transfusions of red blood cells (p = 0.0118) and platelets (p = 0.0470), a significantly higher re-thoracotomy rate (p = 0.0003), significantly prolonged stay in the intensive care unit (p =0.0140), and a longer hospital stay (p = 0.0240).

Conclusions

The use of CytoSorb® for removal of Ticagrelor and Rivaroxaban in emergency open heart operations is a fundamental and safety therapeutical strategy. The data show how this effective method can reduce bleeding complications.

The use of CytoSorb® with a scheduled approach is recommended for life-threatening patients in Ticagrelor or Rivaroxaban therapy undergoing emergency cardiac surgery.

A084

Clinical Use Of CytoSorb® As Adjuvant Therapy During CPB In Patients With Sepsis For Bacterial Endocarditis And Hypothermic Cardiac Arrest

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Introduction

Cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response (SIRS), contributing to vasoplegia, multiorgan dysfunction, and hemodynamic instability. CytoSorb®, an extracorporeal hemoadsorption therapy, remodulates the excess of cytokines and inflammatory mediators, aiming to reduce inflammation and improve clinical outcomes. This study evaluates the impact of CytoSorb® in patients undergoing high-risk cardiac surgeries, particularly in cases of hypothermic cardiac arrest (HCA) and acute bacterial endocarditis (ABE).

Methods

A retrospective study was conducted at Hesperia Hospital, Modena (November 2023 – August 2024), analysing 33 patients undergoing complex cardiac surgery with CPB and CytoSorb® therapy during intra and post-operative, for 24 to 48 hours. Patients were divided into two subgroups: 21 underwent HCA due to acute aortic dissection, and 12 with ABE. The control group included nine patients with aortic dissection and CPB without CytoSorb.

The primary endpoint was mortality. Secondary endpoints included hemodynamic stability (vasopressor requirements and lactate clearance), inflammatory response (C-reactive protein [CRP], procalcitonin [PCT]), level of injury (myoglobin levels), mechanical ventilation duration, and ICU length of stay. Measurements were taken at baseline, 24, and 48 hours postoperatively.

Results

HCA Patients: CytoSorb significantly reduced CRP and PCT levels at 24 and 48 hours ($p<0.05$), while norepinephrine use declined markedly ($p=0.00009$), with discontinuation by 48 hours. Myoglobin levels trended downward within 24 hours ($p=0.1538$), suggesting reduced ischemia-reperfusion injury. Despite these benefits, mortality was 16%, though not statistically significant due to the small sample size.

ABE Patients: CytoSorb led to rapid hemodynamic stabilization, with norepinephrine discontinued by 48 hours. CRP and PCT reductions were significant ($p<0.05$), and lactate levels showed a downward trend ($p=0.15732$), reflecting improved perfusion. All patients survived.

Control Group: Patients without CytoSorb required vasopressor support beyond 48 hours, and inflammatory markers remained elevated longer. No significant differences were observed in ICU stay or mechanical ventilation duration.

Conclusion
CytoSorb reduced inflammation and vasopressor needs, improving hemodynamic stability. The lack of statistical significance in HCA mortality likely reflects the limited sample size rather than a lack of benefit. These results align with previous studies in cardiac surgery. Further multicenter research is needed to confirm CytoSorb's impact and refine patient selection.

A085

Hemoadsorption For Dabigatran Removal In An ECMO Patient: A Case Report On Anticoagulation Management

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Introduction
The management of coagulation in extracorporeal membrane oxygenation (ECMO) patients is particularly challenging due to the need for anticoagulation to prevent circuit thrombosis while minimizing haemorrhagic complications. Direct oral anticoagulants (DOACs), such as Dabigatran, further complicate this balance, particularly in patients with impaired renal function, where drug accumulation can lead to excessive anticoagulation. Unlike vitamin K antagonists, DOACs lack standardized reversal strategies outside of specific antidotes, making urgent anticoagulation modulation difficult. CytoSorb hemoadsorption therapy has been introduced as an effective method for removing DOACs.

Methods
After catheter ablation, a 58-year-old male developed refractory biventricular shock, requiring veno-arterial ECMO support. Laboratory tests revealed excessive anticoagulation due to Dabigatran accumulation (452 ng/mL), exacerbated by acute renal failure. Given the necessity of transitioning to unfractionated heparin for ECMO, an urgent reversion of Dabigatran was required. CytoSorb hemoadsorption was integrated into the ECMO circuit for rapid Dabigatran elimination. Idarucizumab was not administered due to concerns that its effect could induce a hypercoagulable state, requiring ECMO unplanned discontinuation. Coagulation parameters, including thrombin time, aPTT, and Dabigatran plasma levels, were rigorously monitored throughout the treatment course.

Results
Six hours after hemadsorption initiation, pre-cartridge Dabigatran levels had dropped to 43 ng/mL, while post-cartridge levels were 36 ng/mL, indicating effective drug removal.

After 24 hours, a pre-cartridge measurement showed an increase in Dabigatran concentration to 93 ng/mL, while the post-cartridge level was 90 ng/mL. This rise was attributed to redistribution of Dabigatran from peripheral compartments back into the bloodstream. To have an effective drug removal, a second cartridge was started. By the final assessment, Dabigatran plasma concentration had decreased further to 38 ng/mL, a level considered below therapeutic activity.

Conclusions
The use of CytoSorb hemoadsorption therapy successfully facilitated Dabigatran removal in a critically ill ECMO patient with renal impairment. Ultimately, the intervention enabled safe anticoagulation transition to heparin, reducing hemorrhagic risk while maintaining ECMO circuit function. This case highlights the need for dynamic anticoagulation management strategies in ECMO patients with DOAC accumulation and underscores the utility of CytoSorb as an adjunctive therapy in such complex scenarios.

A086

The Role Of CytoSorb® Hemoadsorption In The Perioperative Management Of Patients Undergoing Cardiac Surgery For Aortic Dissection: Impact On Clinical Outcomes

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Introduction
Acute type A aortic dissection (AAD-A) is a surgical emergency often complicated by a systemic inflammatory response due to cardiopulmonary bypass (CPB). This phenomenon is particularly severe in patients with high vasoactive-inotropic needs, who often show unstable hemodynamics and poor prognosis. CytoSorb® is an extracorporeal hemoadsorption device that may help mitigate inflammation by modulating circulating cytokines, potentially improving postoperative outcomes in this vulnerable population.

Methods
A retrospective single-center study analyzed 19 patients undergoing emergent surgery for AAD-A between March and October 2024. Patients were divided based on intraoperative CytoSorb® use. A subgroup of patients with VIS >15 was analyzed for differences in hemodynamic stability (lactate clearance), respiratory function (P/F ratio), and inflammatory response (IL-6 levels).

Results
Among patients with VIS >15, those treated with CytoSorb® had lower IL-6 levels during and after CPB. At the end of bypass, IL-6 peaked at 477 pg/mL in the CytoSorb® group compared to 1250 pg/mL in controls, a 61.8% difference, indicating the effectiveness of cytokines' adsorption. After 24 hours, IL-6 remained 60% lower in the CytoSorb® group (87.1 vs 146 pg/mL), and at 72 hours, IL-6 dropped further to 50 pg/mL compared to 108 pg/mL, marking a difference of 53.7%.

Lactate clearance was also notably better in the CytoSorb® group. At 36 hours post-op, lactate levels were reduced to 1.1 mmol/L, versus 2.75 mmol/L in the control group (40% lower). This trend persisted at 60 and 72 hours.

Improvement in respiratory performance followed a similar trajectory. At 72 hours, the median P/F ratio in CytoSorb® patients was 190, more than double that of the non-treated group (82.5), suggesting a 130% relative improvement in oxygenation.

Conclusions
In AAD-A patients with severe hemodynamic compromise (VIS >15), CytoSorb® hemoadsorption was associated with a markedly reduced inflammatory response, faster lactate normalization, and superior respiratory recovery. These results support the potential of CytoSorb® to modulate postoperative trajectories in high-risk surgical patients. Although mortality differences were observed, the most compelling signals lie in the physiologic stabilization that may underlie longer-term outcome improvements. Larger studies are warranted to validate these promising observations.

A087

Use Of Cytosorb During Cardiopulmonary Bypass And Circulatory Arrest In Acute Aortic Dissection Surgery

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Introduction

This study focuses on evaluating the effect of CytoSorb®, a hemadsorption therapy, on vasoactive and inotropic support in patients undergoing surgery for acute aortic dissection (AAD) with circulatory arrest. The study compares two groups: one treated with CytoSorb® and one treated without it, looking at how this therapy affects the need for vasopressors and inotropes after surgery.

Methods

Cytosorb® Group: 29 patients who underwent AAD surgery with CytoSorb® between May 2022 and June 2024. Non-Cytosorb® Group: 33 patients who underwent AAD surgery between January 2018 and May 2022, without CytoSorb®. No significant differences between the two groups, except for cardiopulmonary bypass temperature and circulatory arrest time (these factors did not significantly affect drug use as per regression analysis). The primary outcome was the change in the vasoactive-inotropic score (VIS), a measure of the degree of hemodynamic support required (i.e., vasopressors and inotropes). The VIS and drug doses were recorded at 8 time points from preoperative to 72 hours post-surgery.

Results

The group receiving CytoSorb® showed lower VIS values at every time point (figure 1), indicating reduced need for vasoactive drugs, with statistically significant differences seen from ICU admission (p=0.026) to 24 hours post-surgery (p=0.029). The VIS showed two peaks after surgery—one early after the discontinuation of cardiopulmonary bypass, and another around 6 hours post-surgery. There were no significant differences between the groups in terms of In-hospital mortality (p=1), Hospital length of stay (p=0.1), Postoperative highest creatinine value (p=0.05).

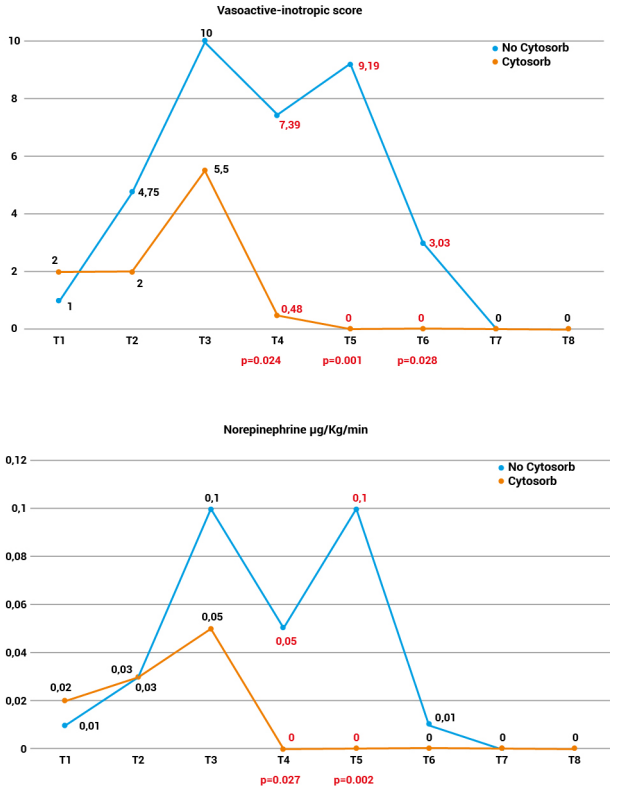

Figure 1 | VIS and NE trend

Conclusion

The study suggests that CytoSorb® may improve hemodynamic stability by reducing the need for vasoactive drugs in AAD surgery patients, as reflected by the lower VIS values in the CytoSorb® group. CytoSorb® may be beneficial in improving hemodynamic stability immediately after complex surgeries like AAD with circulatory arrest by reducing the reliance on vasoactive drugs.

A088

Use Of CytoSorb In Patient With Refractory Vasoplegic Shock

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Introduction

Cardiac surgery, particularly with cardiopulmonary bypass (CPB) and prolonged circulatory arrest, can result in vasoplegia during the post-operative period. In certain cases, vasoplegic shock becomes refractory to conventional treatments, such as vasoconstrictors and fluid therapy, greatly increasing the risk of multiorgan failure and mortality.

CytoSorb®, a hemoadsorption therapy, has emerged as a therapy capable of controlling cytokine storms. This report presents a case of severe postoperative vasoplegic shock effectively treated with an intensive CytoSorb® protocol.

Methods

A 65-year-old man with hypertension, COPD, OSAS, obesity, and a pacemaker underwent a Bentall procedure for ascending aorta and aortic valve replacement, along with myocardial revascularization (LIMA to LAD) and venous grafting to the right coronary artery due to coronary ostial bleeding. The procedure involved prolonged CPB (297 minutes) and aortic clamping (154 minutes). Post-CPB weaning was supported by high doses of norepinephrine (up to 0.20 µg/kg/min) to address significant vasodilation.

Initially, the patient's hemodynamics were stable, but severe vasoplegia soon developed, requiring norepinephrine (up to 0.40 µg/kg/min) and argipressin (0.03 U/min). He became unresponsive to maximal doses of vasopressors and adjunct therapies, including methylprednisolone (200 mg/day) and methylene blue (2 mg/kg infused over 20 minutes).

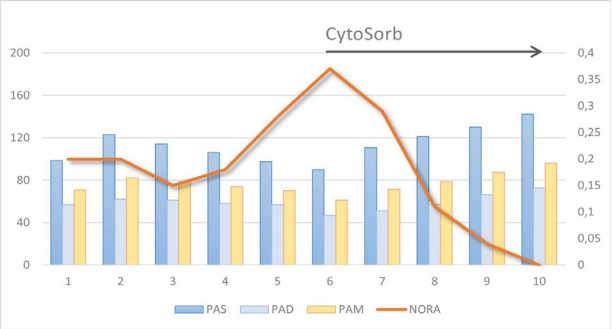

Figure 1 | Hemodynamic parameters before and after use of CytoSorb

Continuous renal replacement therapy (CRRT) combined with intensive CytoSorb® hemoadsorption was initiated. Four CytoSorb® sessions were performed: two 12-hour sessions followed by two 24-hour sessions.

Results

Blood cultures remained negative throughout the hospital stay. CytoSorb® therapy effectively reduced the cytokine storm, improving systemic blood pressure, decreasing pulmonary pressure, lowering lactate levels, reducing vasopressor requirements, and partially restoring diuresis (Figure 1)

Conclusion

For severe vasoplegic shock resistant to high-dose vasopressors, CytoSorb® therapy demonstrated significant hemodynamic improvement, enabling vasopressor discontinuation and systemic perfusion recovery.

This case highlights the potential of CytoSorb® as a critical intervention in refractory vasoplegic shock during cardiac surgery, warranting further validation through randomized controlled trials.

A089

Extracorporeal Blood Purification With CytoSorb® In Patients With Shock: Standalone Circuit Configuration Versus Integrated Use Within Extracorporeal Membrane Oxygenation

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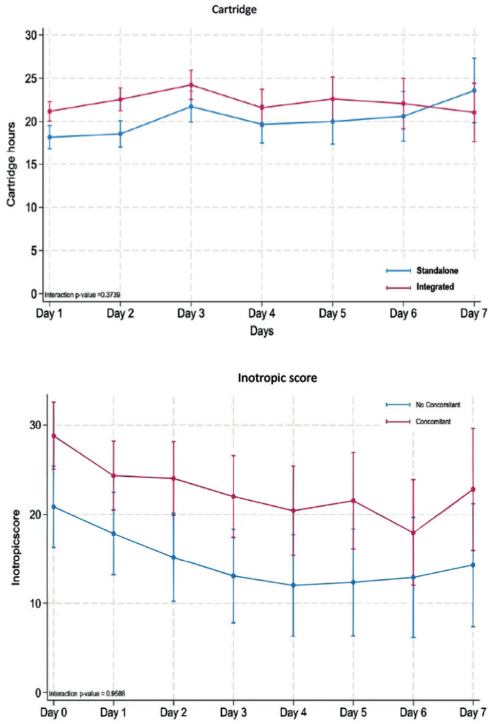

Figure 1 | Comparison of cartridge duration and inotropic score variation during CytoSorb® treatment between the two groups under study

Introduction

Extracorporeal hemoadsorption with CytoSorb® is being increasingly adopted in different critically ill settings to allow for both enhanced organ protection and control of inflammation derangement. We evaluated the characteristics and performances of two different CytoSorb® circuit configurations to generate data that may contribute to optimize and inform clinical practice.

Methods

We performed a secondary analysis of the largest currently available cohort of critically ill patients undergoing extracorporeal hemoadsorption with CytoSorb® at a referral center (doi: 10.1159/000530872). Data from 148 patients (41%) receiving CytoSorb® as a standalone circuit were compared to data from 211 patients (59%) who had the CytoSorb® cartridge integrated within the ECMO circuit.

Results

Patients with concomitant ECMO were admitted to ICU mainly for cardiac arrest or cardiogenic shock (73.9%) and underwent hemadsorption with CytoSorb® to mitigate inflammatory derangement, while patients without contemporary ECMO were admitted for either cardiogenic shock or after cardiac surgery (77.3%) and the prevalent indication for CytoSorb® treatment was hyperbilirubinemia (p<0.001). Patients in the ECMO group exhibited more severe shock and higher inotropic load at baseline (20 (10-35) vs 15 (5-30), p=0.001). 80.3% were administered renal replacement therapy, with a prevalence in patients undergoing concomitant ECMO (p<0.001). Patients received a median of 2 CytoSorb® cartridges within a single cycle. The duration of each cartridge and CytoSorb® efficacy, as documented by improvement in shock and organ failure laboratory parameters and intropic score reduction (Figure 1), was comparable in both groups. ICU and hospital survival were higher in patients treated with CytoSorb® as a standalone circuit (54.1% vs 34.1%, p<0.001 and 49.3% vs 30.8%, p<0.001, respectively) (Figure 1).

Conclusions

CytoSorb® treatment proved safe and effective in both configurations. Despite great inter-group diversity at baseline and in their clinical outcomes, the choice of CytoSorb® configuration had no impact on cartridge performance and duration.

A090

Efficacy Of Hemoadsorption Therapy In The Dabigatran Removal: A Case Report

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Introduction

Dabigatran etexilate is a direct thrombin inhibitor that provides anticoagulant effects without requiring dose adjustments or periodic monitoring. Its half-life is dose-independent, estimated at 12–14 hours, with a distribution volume of 50–70 L, and approximately 80% is excreted renally.

Extracorporeal therapies combined with Cytosorb, the only adsorbent cartridge certified for whole-blood removal of bilirubin, cytokines, myoglobin, Ticagrelor, and Rivaroxaban, may be a useful approach also for Dabigatran removal.

Cytosorb is recommended by ESAIC guidelines for the removal of Ticagrelor and Rivaroxaban in anticoagulated patients undergoing emergency surgery.

Methods

An 85-year-old man on dabigatran 110 mg twice daily for one month due to permanent atrial fibrillation presented to the emergency department after a syncopal episode caused by acute anemia secondary to enterorrhagia. On clinical examination, the patient presented with asthenia, BP 105/40 mmHg, HR 60 bpm, aPTT ratio 1.88.

He was treated with Idarucizumab for suspected dabigatran overdose. While rectal bleeding appeared to cease, anuria persisted. Continuous veno-venous hemodiafiltration (CVVHDF) without heparin was initiated but led to circuit obstruction, requiring intermittent hemodialysis (BHD). Subsequently, massive rectal bleeding occurred; with an aPTT ratio of approximately 1, Idarucizumab was administered again.

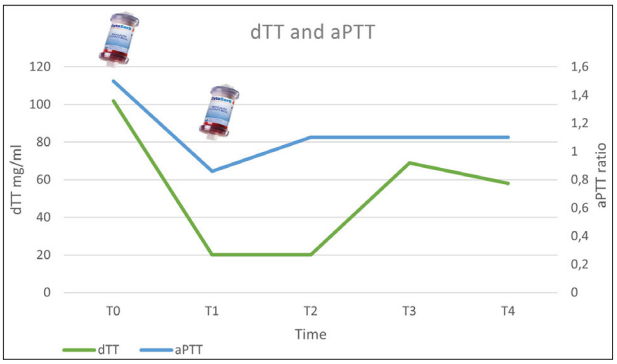

Figure 1 | dTT and APTT trend

The diluted thrombin time (dTT) was 102 ng/mL despite dabigatran discontinuation for three days. Continuous renal replacement therapy (CRRT) with Cytosorb® was then initiated.

Results

After 24 hours of Cytosorb® therapy, dTT decreased to 20 mg/mL and aPTT ratio to 0.86 (Fig.1) . Treatment continued for 48 hours, after which dialysis was discontinued due to resumed diuresis. However, after 24 hours, Dabigatran levels rose again (dTT = 69 ng/mL) before spontaneously declining with renal function recovery.

Conclusions

The combination of Idarucizumab and Cytosorb® effectively reduced plasma Dabigatran levels. However, the drug's large volume of distribution may cause post-dialysis rebound. Cytosorb® efficiently removes Dabigatran, but complete clearance requires some days of treatment.

A091

Hemoperfusion With CytoSorb In Pediatric Age: A Valid Therapeutic Option In The Treatment Of Refractory Cardiogenic Shock In Septic Patients

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Introduction

Refractory cardiogenic shock is one of the main causes of death in pediatric age, requiring timely diagnosis and treatment, especially in cases of overlap with septic shock. At the base of myocardial and multi-organ dysfunction, the "cytokine storm" plays a crucial role. In support of standard immunosuppressive treatments, hemoperfusion with CytoSorb presents itself as an additional therapeutic option. CytoSorb is a cartridge composed of polystyrene-divinylbenzene beads, whose purpose is to remove medium molecular weight molecules (≤ 55 kDa), including multiple cytokines.

Methods

We report the case of a 5-year-old girl who arrived at the emergency room tachycardic, oliguric, and febrile, with otalgia, latero-cervical lymphadenopathy, and hypotension, associated with neutropenia and elevated levels of PCR, PCT, and NT-proBNP. In her medical history, a previous episode of acute pharyngitis successfully treated with corticosteroids and antibiotic therapy. The echocardiogram showed severe biventricular dysfunction with 15% ejection fraction (EF). The CT scan showed an extensive tonsillar abscess and upper lobe pneumonia. Due to positivity to the urinary antigen of Streptococcus, a fulminant infection by Streptococcus dysgalactiae was diagnosed, with rapid evolution into septic and cardiogenic shock and a Predicted Death Rate (PDR) of 86.4%. Upon finding metabolic acidosis and hyperlactatemia, hemoperfusion with CytoSorb was initiated, associated with methylprednisolone and immunoglobulins.

Results

The first two cartridges were changed every 6 hours, the last one after 12 hours. 12 hours later, an increase in EF to 38% was noted, further improved to 50% after 24 hours. Additionally, there was a reduction in lactate, PCR, NT-proBNP, PELOD-2 score, and PDR to <20%. 3 and 6 days after the start of hemoperfusion, adrenaline and dobutamine were respectively discontinued.

Conclusions

CytoSorb proved to be effective as supportive treatment in septic shock with multi-organ involvement, even in pediatric patients, especially where standard therapies alone fail.

A092

Hemadsorption In Cardiogenic Shock: A Case Report

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Introduction

Cardiogenic shock (CS) is a life-threatening condition characterized by severe myocardial dysfunction and inadequate tissue perfusion. Hypoperfusion promotes to systemic inflammation, and cytokines release can further exacerbate multi-organ failure.

When conventional therapies (inotropes, vasopressors, intra-aortic balloon pump) fail, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) provides mechanical circulatory support.

In this setting, hemoadsorption with CytoSorb® during VA-ECMO has emerged as a promising adjunctive strategy.

We describe the case of a patient treated with CytoSorb® during VA-ECMO support.

Methods

A 56-year-old male developed post-cardiotomy cardiogenic shock following aortic valve replacement and mitral valve repair.

He presented with markedly elevated inflammatory markers and was treated with VA-ECMO (*ECMOlife, Eurosets*) combined with hemoadsorption for 24 hours.

The CytoSorb® cartridge was integrated into the VA-ECMO circuit under systemic heparin anticoagulation.

Results

VA-ECMO was initiated immediately after surgery. Due to clinical deterioration, hemoadsorption was started, resulting in significant laboratory improvements :

CRP: 7.22 → 4.48 mg/L; PCT: 11.3 → 4.78 ng/mL; Lactate: 1.7 → 0.9 mmol/L; CK-MB: 13.7 → 8.49 U/L;

AST: 146 → 100 U/L; ALT: 36 → 38 U/L; Bilirubin: 4.33 → 3.25 mg/dL; hs-TnT: 2037 → 1429 ng/L.

(Values pre- vs post-treatment shown in Figure 1).

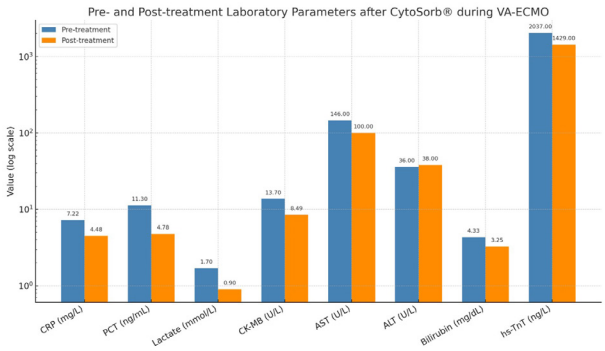

Figure 1 | Pre- and post- treatment biochemical analysis

Conclusion

CytoSorb® hemoadsorption appears to be a safe adjunctive therapy with potential benefits in modulating inflammation and organ dysfunction.

It may represent a therapeutic option for cardiogenic shock patients supported with VA-ECMO.

A093

Hemodynamic And Metabolic Impact Of CytoSorb In ECMO-Supported Patients

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Introduction

In the cardiothoracic intensive care setting, patients receiving extracorporeal membrane oxygenation (ECMO) often present severe inflammatory responses and multi-organ dysfunction, for which hemofiltration has emerged as a potential adjunctive therapy to modulate the inflammatory milieu and support hemodynamic stability. The aim of this study was to assess the efficacy of hemofiltration using CytoSorb in terms of clinical outcomes and mortality.

Methods

Demographic data and hemodynamic parameters were retrospectively collected from patient records. Baseline data included patient demographics, reason and dates of ICU admission and discharge, as well as the start date and duration of CytoSorb therapy. Data were recorded

at ICU admission, at baseline (prior to CytoSorb initiation), and 24 hours after therapy. The vasoactive inotropic score (VIS) was used to objectively quantify the level of hemodynamic support required.

We included 11 ECMO-supported patients (64% male) with a mean age of 55 ± 9 years at the time of ICU admission. The patients were admitted to the ICU: post-valve replacement (36%); post-endovascular pulmonary artery intervention (27%); and chronic thromboembolic pulmonary hypertension (18%). The remaining two patients were admitted to the ICU for acute respiratory failure due to pneumonia and post-bilateral lung transplantation.

Results

The mean length of stay (LoS) was 46 ± 26 days, and the ICU mortality rate was 36%. A total of 55% of patients demonstrated a reduction in VIS and lactate levels 24 hours after CytoSorb therapy, suggesting a positive clinical response with decreased need for inotropic and vasopressor support. However, a subset of patients showed an increase in VIS and lactate levels at 24 hours, indicating hemodynamic deterioration or lack of treatment efficacy.

No CytoSorb-related complications were observed.

Conclusion

These preliminary data suggest a potential benefit of CytoSorb use in ECMO patients in the cardiothoracic ICU setting across different admission diagnoses, particularly in terms of reducing VIS and lactate levels. However, the heterogeneity of the study population and the presence of numerous confounding variables limit the ability to draw definitive conclusions. Further studies involving more homogeneous patient populations are needed to better evaluate the clinical impact of CytoSorb therapy and to clarify its role within specific diagnostic subgroups.

A094

Feasibility Of Intraoperative And Postoperative CytoSorb Hemoadsorption In Cardiac Surgery For Infective Endocarditis: A Case Report

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Introduction

Infective endocarditis remains a significant challenge in cardiac surgery, particularly due to the associated systemic inflammatory response and the need for complex surgical interventions. Managing perioperative and postoperative inflammation is crucial for improving patient outcomes.

Methods

We report the case of a 79-year-old male patient with a history of aortic valve replacement surgery in 2015, who was admitted to the emergency department with a diagnosis of infective endocarditis. The patient underwent a “Commando” procedure, involving replacement of the mitral-aortic junction. To control the systemic inflammatory response, CytoSorb hemoadsorption therapy was used intraoperatively during 182 minutes of cardiopulmonary bypass (CPB). Concurrently, an ApherCapmachine was prepared with a dedicated circuit. The Cytosorb cartridge was washout at the end of CPB and insert in the ApherCapMachine. At the end of the surgery procedure a 13 Fr, 20 cm coaxial catheter was placed and connected to the ma-chine. Postoperatively, CytoSorb therapy was continued for 9 hours, with continuous flow of 250 ml/min. (Fig. 1).

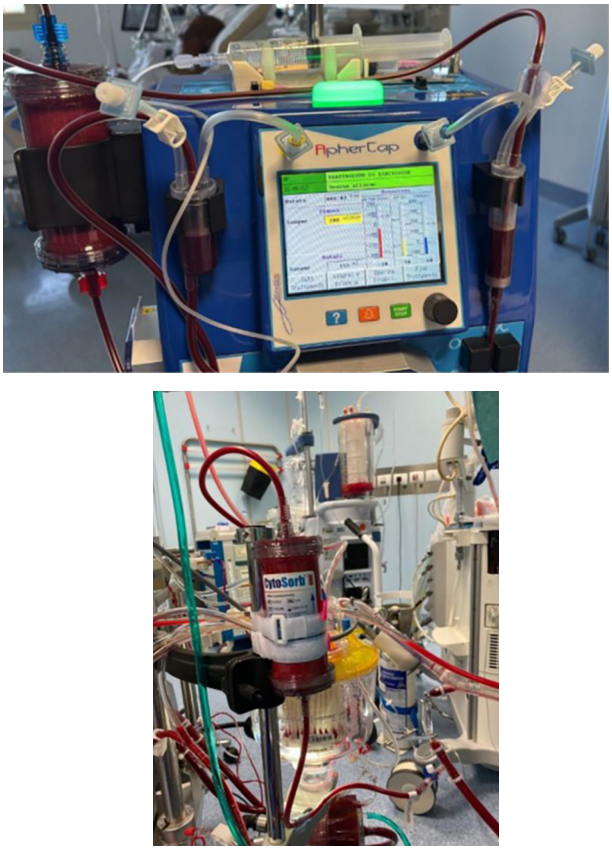

Figure 1 | CytoSorb set up with ApherCapmachine

Results

ApherCapprocessed a total of 135 liters of blood. Interleukin-6 (IL-6) levels were measured as the primary inflammatory marker. Values were as follows:

- Pre-CPB: 60.4 pg/mL
- After 1 hour of CPB with CytoSorb (pre-filter): 109 ng/L
- After 1 hour of CPB with CytoSorb (post-filter): 101 ng/L
- Post-CPB: 1235 ng/mL
- End of CytoSorb with ApherCaptreatment: 1720 ng/L
- The final IL-6 level with CVVC + CytoSorb: 2690 ng/L

Conclusion

This case highlights the feasibility and adaptability of combining intraoperative and postoperative CytoSorb therapy for managing the inflammatory response during cardiac surgery for infective endocarditis. The observed rise in IL-6 levels may result from systemic measurements that overlook ongoing IL-6 production, although pre/post sorbent data has demonstrated CytoSorb effectiveness. Further studies are warranted to optimize the timing, duration, and integration of hemoadsorption.

A095

Use Of Hemoadsoprtion After Frozen Elephant Trunk For An Ascending Aortic Aneurysm

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Introduction

An ascending aortic aneurysm is a dilation of the upper portion of the aorta and often requires open surgical repair. CPB and aortic cross-clamping in aneurysm surgery can trigger a massive release of pro-inflammatory cytokines (e.g., IL-6, TNF-α). Hemoadsorption has been associated with reduced vasopressor need postoperatively due to lower inflammation-driven vasodilation.

Methods

We present the case of a patient with an ascending aortic aneurysm, aortic arch, and proximal descending thoracic aorta, who underwent cardiac FET (Frozen Elephant Trunk) surgery. Postoperatively, she was admitted from the operating room following FET. She arrived under analgesia and was awaiting curarization. The patient was intubated and on mechanical ventilation in controlled mode. Hemodynamics were supported with continuous infusions of epinephrine, dobutamine, norepinephrine, and vasopressin. Due to hypovolemia, she received crystalloid infusion. CRRT was started with a single Cytosorb cycle to improve hemodynamics and reduce vasopressor requirements.

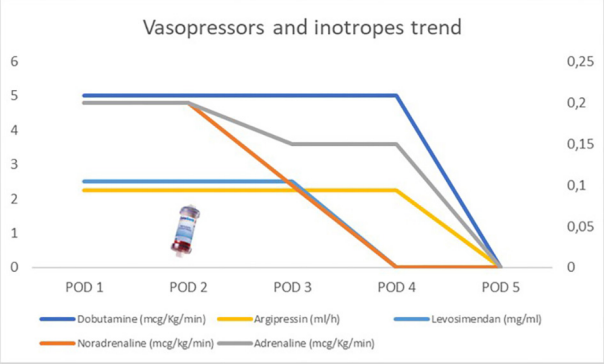

Figure 1 | Vasopressors and inotropes trend after FET

Results

Within the first few days postoperatively, vasopressor doses were significantly reduced. By the fifth postoperative day, the patient's hemodynamic status had stabilized, and no further support with vasoactive amines was required (see figure 1). This improvement coincided with ongoing critical care management and the initial application of hemoadsorption therapy.

Conclusions

This case highlights the potential benefit of CytoSorb hemoadsorption in managing severe postoperative inflammation and hemodynamic instability following complex aortic surgery. Its use was associated with reduced vasopressor requirements and improved stability, suggesting a valuable adjunct in the perioperative care of high-risk cardiovascular surgical patients.

A096

Ultrafiltration Nefrocardiocare, Our Experience

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Introduction

In advanced forms of congestive heart failure refractory to maximal medical therapy, patient management is extremely complex and requires a multidisciplinary approach and more aggressive therapies.

In our experience we have submitted such patients to nephrocardiocare ultrafiltrative treatment.

Methods

Fourteen patients aged > 65 years with clinical and laboratory signs of cardiorenrenal decompensation were enrolled, presenting at the time of admission:

- EF between 35 and 55%
- a weight gain of at least 3 kg in the previous month
- signs of overload to instrumental investigations (pleural and/or endoabdominal effusion/anasartic state)
- dyspnea (stratified through dedicated score)
- renal function III-IV stage sec KDOQI at the baseline, submitted to diuretic stimulus in the first 24 hours of about 129-150 mg/day

They have been subjected to standard medical therapy since entry and subsequently, based on the clinical and laboratory response, they were proposed treatment with UFI nefrocardiocare, in single or multiple session, with a liquid removal greater than 2 l/session (nb. To reduce the risk of hypovolemia and consequent renal damage induced by hypoperfusion the recommended total loss should not be more than 75% of the estimated PC input). The parameters monitored were: PC +/- BIA, renal function indices, serum electrolytes, Hb and HCT, dyspnea score, PA detected respectively at input, 48h, 96h, dimission and first mount later. The UFI sessions necessary to restore the state of compensation and the days spent in the hospital were subsequently evaluated.

Results

For each patient the improvement of dyspnea (according the score) and of the state of congestion (PC/BIA) was documented already at 48H, the achievement of a more stable renal function over time, and, last but not least, the reduction of recovery. Significant longterm changes were also observed for systolic blood pressure, Hb, Na and dyspnea.

Conclusions
Our study demonstrates that the choice of UFI as firstline treatment in patients with cardiorenrenal decompensation leads to greater short-term outcomes and greater long-term stabilization of cardiorenrenal function with reduced hospitalization rate. The Nefrocardiocare treatment has a valuable impact in improving and stabilising long-term renal function and dyspnea of these patients.

Autoimmune Disorders

A097

Efficacy Of Adsorptive Cytapheresis In The Treatment Of Inflammatory Bowel Disease: A Case Series

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Introduction
Adsorptive cytapheresis (AC), or leukocytapheresis, is a therapy where a patient's blood passes through a device containing a column that selectively adsorbs activated monocytes, granulocytes, and lymphocytes. The remaining leukocytes and blood components return to the patient.

AC is a non-pharmacological treatment for Inflammatory Bowel Diseases (IBD), including, Ulcerative Colitis (UC) and Crohn's Disease (CD). The 2023 American Society for Apheresis guidelines classify AC as Category II, 1B for UC and Category III, 1B for CD.

While the exact cause of IBD remains unclear, inflammatory cytokines like TNF-α are known to contribute, making them key treatment targets.

Since these cytokines originate from leukocytes, leukocytapheresis helps reduce their activation.

When activated leukocytes are depleted, the patient's immune system can readjust to normal function or at least improve the efficacy of pharmacological therapy.

Since AC removes elements from the body, it has not been associated with dependency, refractoriness, or safety concerns.

Methods
Case series of 7 patients affected by UC. Every one of them was treated by 7 to 15 times in a time range of 2-36 months (2023-2025).

The duration of each individual treatment is approximately one hour, using the Leucapher® device and LA 25® filter at a blood flow rate of 30 ml/min.

Results
All patients exhibited good clinical response, with a significant improvement in symptoms as a reduction in diarrheal episodes, with the restoration of normally formed stools, indicating an improvement in intestinal function. Notably, in several cases, disease remission was observed, with symptom resolution and quality of life improvement.

A particularly significant aspect emerging from the study was that RBC values remained virtually unchanged throughout the entire treatment period, highlighting the absence of anemia in treated patients.

This finding further reinforces the safety of AC as a therapeutic approach with no relevant adverse effects.

Conclusions
These results suggest that AC may represent a safe and effective therapeutic option for patients with UC, particularly for those who do not respond adequately to conventional pharmacological therapies or who wish to reduce the use of immunosuppressive drugs.

A098

Efficacy Of Adsorptive Cytapheresis In The Treatment Of Neutrophilic And Autoinflammatory Dermatoses: A Case Series

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Introduction

Neutrophilic and Autoinflammatory Dermatoses are a group of skin diseases characterized by neutrophil-mediated inflammation without a primary infection. They share pathogenetic mechanisms linked to dysregulation of the innate immune system and may be associated with systemic diseases.

Adsorptive Cytapheresis (AC) can be considered as an emerging strategy for severe or treatment-resistant cases.

It controls inflammation by removing pro-inflammatory mediators, reducing cytokines like TNF-α, IL-1β, and IL-6. It also limits tissue damage by eliminating hyperactivated neutrophils. Its immunomodulatory effect restores balance, reducing autoantibodies and immune complexes, improving disease control.

Methods

Case series of 4 patients affected by Pyoderma Gangrenosu, Hidradenitis Suppurativa, Acne Conglobata, Recurrent Forunculosis.

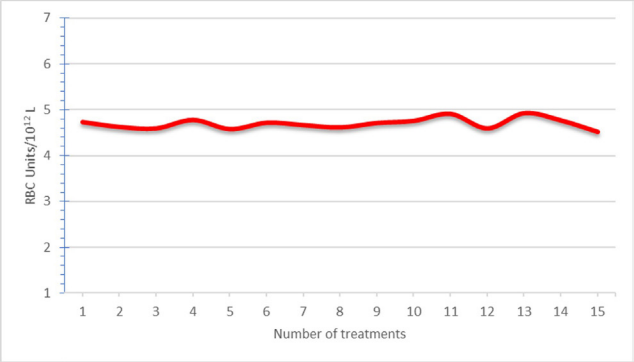

Figure 1 | RBC levels

Every one of them was treated by 12 to 15 times in a time range of 16 months. The duration of each single treatment is approximately one hour, using the Leucapher® equipment and LA 25® filter at a blood flow of approximately 30 ml/min.

Results

All patients exhibited good clinical response, with a significant improvement in skin lesions and quality of life improvement.

A particularly significant aspect emerging from the study was that RBC values remained virtually unchanged throughout the entire treatment period, highlighting the absence of anemia in treated patients (Figure 1).

This finding further reinforces the safety of leukocytapheresis as a therapeutic approach with no relevant adverse effects.

Conclusion

Neutrophilic and autoinflammatory dermatoses represent a group of disorders with a broad spectrum of clinical manifestations and associations with systemic diseases. AC is emerging as an innovative option for severe or refractory cases, providing a targeted approach to removing inflammatory mediators and modulating the immune response. Further investigation into the pathogenesis and the development of targeted therapies, particularly through the use of biological agents and therapeutic apheresis, represent a possible direction for more effective management of these conditions.

A099

Results Of Double Filtration Plasmapheresis (DFPP) For Immuno-Modulatory Treatment Of Neurological Diseases And For Desensitization Before AB0-Incompatible Kidney Transplant

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Introduction
Therapeutic plasma exchange is recommended by the American Society For Apheresis as a standard of care for some neurological diseases (categories I to III, grades 1 to 2) and for AB0-incompatible solid organ transplant (category II, grades 1B to 2B). Double filtration plasmapheresis (DFPP) is a selective plasma exchange technique that removes high-molecular-weight molecules, minimizing albumin loss.

Methods
Between October 2022 and January 2025, ten patients underwent DFPP treatment with Plasmapher/Apherlungs system at Santissima Annunziata Hospital, Savigliano (Italy), ASL CN1. Nine out of ten patients were treated with DFPP for neurological diseases ranging from acute inflammatory demyelinating polyneuropathy (56% of the patients) to autoimmune encephalitis, myasthenia gravis, para-neoplastic encephalopathy and optic neuro-myelitis (11% each). One patient underwent DFPP for desensitization before an AB0-incompatible kidney transplant. Median patients' age was 50 years. Median number of DFPP sessions was four, ranging from 2 to 6 sessions on alternate days. The medium volume of treatment was 1.5 times the plasma volume. Plasma fractionator Eva-Flux 3A20 was used. Anticoagulation was obtained by continuous administration of unfractionated heparin. Central venous catheters were placed before DFPP in all the patients treated for neurological diseases, whereas a pre-existing arteriovenous fistula was suitable for the patient undergoing desensitization.

Results
Nine out of ten patients completed the treatment. In a single case DFPP was prematurely discontinued because of a rapid onset heparin-induced thrombocytopenia that presented with extracorporeal circuit clotting and required heparin withholding, anticoagulant treatment and delayed removal of the central venous catheter. Neither minor nor major bleeding events occurred. Iatrogenic hypoalbuminemia was mild and did not require any correction. Treatment response was judged by neurology consultants. Effectiveness of DFPP in desensitization was assessed by pre- and post-procedural monitoring of haemolysin and anti-AB0 immunoglobulin titres.

Conclusion
DFPP is a promising, therapeutic option for immune-mediated, neurological diseases and for desensitization before AB0-incompatible kidney transplant. In our case series, all the patients obtained significant clinical benefit or adequate removal of anti-erythrocyte antibodies. No life-threatening complications occurred, although a case of heparin-induced thrombocytopenia compelled to premature stop of DFPP. Overall, our results prompt further use of DFPP for immuno-modulatory treatment.

A100

Treatment Of Refractory Myasthenia Gravis Via Double-Filtration Plasmapheresis

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Introduction
Myasthenia Gravis (MG) is an autoimmune disease characterized by impaired neuromuscular transmission, with severe manifestations including respiratory difficulty and motor deficits. Double-Filtration Plasmapheresis (DFPP) sessions are useful for reducing antibody titer when pharmacological therapy is ineffective.

Methods
An 83-year-old patient with type III Myasthenia Gravis, seropositive for AChR and Anti-MuSK antibodies, was admitted to the neurology department in December 2023 for high-dose corticosteroid treatment. Due to an inadequate therapeutic response, Eculizumab 900 mg was initiated, without a favourable outcome.

In February 2024, the patient's condition worsened, necessitating endotracheal intubation (IOT) and admission to the intensive care unit. Considering the criticality of his neurological condition, and assessing blood antibody levels (AChR RIA method 8.40 nmol/L; Anti-MuSK RIA method <0.01 nmol/L), a cycle of three DFPP sessions on alternate days was prescribed.

Results
After the first treatment, immediate clinical improvement was observed: the patient was awake and cooperative, intubated with good respiratory dynamics, and hemodynamically stable. He exhibited marked hyposthenia of the orbicular muscles, could lift his head a few centimetres for a few seconds, and maintained the Mingazzini I position for about 5 seconds with no spontaneous lower limb movements.

Following the second session, a further decrease in antibody titers was noted, along with progressive improvement in motor deficits: AChR RIA method 6.80 nmol/L; Anti-MuSK RIA method <0.01 nmol/L. The patient was awake and cooperative, undergoing weaning from IOT, following simple commands, lifting his head 20° from the bed, the right upper limb 120°, and the left upper limb 30°.

With the final treatment, a halving of baseline autoantibody levels was observed: AChR and Anti-MuSK 4.30 nmol/L and <0.01 nmol/L, respectively.

A total of 3500 ml of plasma were treated for each procedure. There was no need for PFC transfusion, and albumin levels remained stable throughout the sessions.

Conclusions
In this clinical case of Myasthenia Gravis refractory to pharmacological treatments, the application of the DFPP technique proved to be safe and effective in reducing antibody titers and improving the patient's neurological condition.

A101

Pure Ultrafiltration As A Therapeutic Strategy In Haemodialysis Patients With Volume Overload: A Prospective Pilot Study With Cardiosmart Equipment

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Introduction
Fluid overload in patients treated with chronic haemodialysis is a frequent condition that develops due to an imbalance between fluid and salt intake and ultrafiltration. This situation is particularly common among patients with heart failure - a frequent complication of chronic kidney disease (CKD) - in whom the ultrafiltration rate is often limited to prevent intradialytic adverse events.

Fluid overload is a known risk factor for mortality and adverse cardiovascular events. To counter this, additional haemodialytic treatments are often administered.

However, these supplemental treatments may be harmful due to two main reasons: (1) not only ultrafiltration but also solute shifts contribute to hemodynamic instability; and (2) the risk of haemodialysis overdosage, especially in frail patients, must be considered.

For these reasons, pure ultrafiltrative treatments are hypothesized to be beneficial and may represent a safer alternative in selected patients.

Methods
Conduction of an explorative, monocentric, prospective clinical trial.

Inclusion criteria
Patients with CKD on chronic haemodialysis three times per week who meet at least one of the following:

- Persistent positive delta on dry weight after dialysis sessions for at least one week

or

- Need for two or more supplemental dialysis treatments within the last 30 days.

Exclusion criteria:

- Severe hyperkalaemia (>6.5 mmol/L) at screening despite maximal medical therapy,
- Previous adverse reaction to the dialysis membrane,
- Current hospitalization for sepsis, acute coronary syndrome, or decompensated heart failure.
- Eligible patients will receive, in addition to their regular dialysis schedule, a supplemental pure ultrafiltration session using Medica Cardiosmart device for a duration of one month.

The following parameters will be assessed after one month of treatment:

- Median delta on dry weight
- Change in dry weight
- Incidence of intradialytic hypotension
- Serum potassium, creatinine and urea levels
- Serum proBNP levels,
- Mortality.

Results
Results will be available after completion of data collection and analysis.

Conclusions
This study aims to evaluate the clinical utility and safety of pure ultrafiltration using Cardiosmart equipment in chronic haemodialysis patients with persistent fluid overload. By avoiding solute shifts and reducing treatment burden, this approach may offer a viable and safer alternative to standard supplemental haemodialysis, particularly in frail populations.

A102

Treatment, With Apheresis Technique Of Cascade Filtration, Of Iatrogenic Hypertriglyceridemia In A Patient Affected By ALL

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Introduction
Severe hypertriglyceridemia has been identified, according to a recent international document, with values higher than 882 mg/dL. In this case report, the clinical case of a patient affected by ALL (Acute lymphocytic leukaemia) is described, in which hypertriglyceridemia arises following therapy with Peg-ASP (Pegylated-Asparaginase).

Methods
The patient, D.A., 49 years old, male, is already known to our hospital as a patient affected by ALL for which he is followed by the Hematology department. On 16/08, following an evolutionary finding of the pathology, he is included in the therapeutic protocol which includes, among other things, therapy with PEG-ASP.

A few days later, he developed severe hypertriglyceridemia with values of 1865 mg/dl. Drug therapy was started in association with a selective plasmapheresis procedure (cascade filtration) using the Fresenius Kabi Amicus cell separator and the Aferetica Plasmapher Apherlungs system with an associated EVALUX 5A20 filter.

Results
After two days, the patient underwent blood tests and an ultrasound scan. The latter excluded the presence of organ damage and the triglyceride value was reduced by approximately 80% (416 mg/dl). The control parameters following the apheresis treatment were also within acceptable ranges; at the dosage of Fibrinogen, a decrease of about 40% is found compared to the average values found in determinations prior to the apheresis procedure before the start of therapy with PEG-ASP.

Conclusions
The reported case demonstrates how, the careful monitoring of the side effects of pharmacological therapies associated with the rapid involvement of the various specialist figures as well as the use of the right therapeutic strategy, can produce positive effects in a short time, such as to avoid even severe complications, with therapeutic techniques almost free from important side effects.

A103

Double Filtration Plasmapheresis In Guillain-Barré Syndrome: Clinical Experience And Rationale In A Complex Case

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Introduction
Guillain-Barré Syndrome (GBS) is an autoimmune disorder affecting the peripheral nervous system, typically presenting with acute flaccid paralysis, although several variants have been described. Pharmacological treatment alone is not always effective and often requires combination with therapeutic apheresis, which allows the removal of target molecules from the plasma—such as autoantibodies responsible for the patients' clinical presentation.

Methods

A 58-year-old female patient, with a history of hypertension, overweight, previous left thalamic ischemic stroke, and atheromatosis of the supra-aortic trunks, presented to the emergency department with hand paresthesias, dysarthria, headache, and elevated blood pressure. The following day, she developed left facial asymmetry and progressive dysphagia, followed by cardiac arrest due to ventricular fibrillation, successfully treated with ACLS manoeuvres and defibrillation. She was transferred to the ICU, where, upon the first neurological window, she was found to be in a deep coma, with absent brainstem reflexes, anisocoric mydriasis, global areflexia, and no spontaneous respiratory drive.

Lumbar puncture revealed albumin cytological dissociation, supporting the diagnosis of Guillain-Barré Syndrome. During the four-month hospitalization, the patient underwent three 5-day courses of IVIg. Additionally, two cycles of double filtration plasmapheresis (DFPP) were performed, each consisting of four alternate-day sessions, using the Plasmapher® device and EvaFlux® 3A filter (mean plasma flow of 20 mL/min; approximately 2.5–3.0 liters of plasma treated per session).

Results

At eight months from symptom onset and following four months of neurorehabilitation, the patient has recently been decannulated, has regained phonation, and is able to eat orally, though not yet independently. She has recovered sensitivity and motor function in all four limbs, though ambulation is still not possible. A reduction in visual acuity is present, with the cause still under investigation, but no evident cognitive impairment has been observed.

Conclusion

DFPP in Guillain-Barré Syndrome facilitates the removal of circulating autoantibodies and immune mediators responsible for peripheral nerve damage, helping to interrupt the autoimmune process and promote neurological recovery.

The choice of DFPP over conventional plasma exchange (PEX) was guided by limited plasma availability and a lower risk of complications, with comparable long-term therapeutic outcomes.

A104

Use Of Immunoadsorption As Therapy In A Patient With Goodpasture's Syndrome: Case Report

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Introduction

Anti-GBM disease is a rare and rapidly progressive autoimmune condition in which early removal of circulating autoantibodies is crucial to prevent irreversible organ damage. Therapeutic apheresis—mainly plasma exchange (PEX) and immunoadsorption—is central to achieving rapid antibody clearance. While PEX is more commonly used, immunoadsorption offers more selective IgG removal with minimal plasma volume loss. Despite its advantages, it remains underutilized due to limited availability and experience. Wider use may improve outcomes in selected patients.

Methods

We describe a 78-year-old man admitted with sub nephrotic proteinuria (2.8 g/24h), progressive renal function decline over six months, and recent outpatient c-ANCA positivity. On admission, serum creatinine was 2.5 mg/dL (eGFR 20 mL/min). The patient also reported fatigue, exertional dyspnea, and dry cough. Chest X-ray revealed bilateral basal infiltrates suggestive of alveolar involvement. During hospitalization, ANCA testing turned negative, but anti-GBM antibodies were positive.

Due to poor peripheral access, a femoral central venous catheter was placed. Immunoadsorption was chosen over PEX to improve efficacy and preserve the hospital's limited plasma and albumin stocks. Treatment was performed with Evaflux 2A columns.

Results
Seven immunoadsorption sessions led to complete anti-GBM antibody clearance. Renal function slightly improved (creatinine stabilized at 2.0 mg/dL), and respiratory symptoms resolved. Chest imaging showed marked improvement. Corticosteroids and anti-CD20 monoclonal antibody were administered concurrently. The patient reported improved quality of life and resumed daily activities.

Conclusion
This case demonstrates the effectiveness and tolerability of immunoadsorption in anti-GBM disease, especially when rapid antibody removal is needed and plasma resources are limited. It may be considered a valid alternative to PEX in selected clinical scenarios.

A105

Double Filtration Plasmapheresis For Patients With Autoimmune Neurological Disorders In ICU: A Case Series

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Introduction
Neurological autoimmune disorders may involve any part of the nervous system and can lead to demyelination or synaptic transmission impairment (1). B-cells have a key role in the pathophysiology, as they produce auto-antibodies (2). Plasmapheresis is a good tool for the treatment of these conditions. Double Filtration Plasmapheresis (DFP) is characterized by two kinds of filters with different pores size: a plasma separator (which separates blood into plasma and blood cells) and a plasma component separator (which separates plasma into large and small molecular weight components). Large molecular components, as immunoglobulins and cytokines are discarded, while small ones are returned to patient (3-4).

Methods
The Authors of the present study retrospectively analyzed patients affected by neurological autoimmune disorders, treated in Bologna IRCCS Intensive Care Unit, which received DFP. The Medical Research Council's (MRC) scale (range 0-60) was used to evaluate impaired muscular function, pre and post DFP treatment. Quantitative Myasthenia Gravis (QMG) scale (range 0-39) was used for patients affected by that disease. A t-test was performed to evaluate differences between these scales before and after DFP treatment.

Results
The enrolled population was composed by 9 patients, 3 females and 6 males, mean age was 55.33 (standard deviation, SD $\pm$23.09). 3 patients were affected by Guillain-Barré syndrome, 3 by autoimmune encephalopathy, 1 by autoimmune myelopathy, 2 by myasthenia gravis. DFP was used as first line of treatment in 55.55% of patients. 8 patients were submitted to invasive mechanical ventilation; 1 patient underwent non-invasive ventilation (patient with myasthenia gravis). The mean duration of mechanical ventilation was 24.55 days (SD $\pm$25.42); 8 out of 9 patients returned to spontaneous breathing. MRC was measured in 7 out of 9 patients: the pre- and post-treatment mean difference was 14.43, with a p-value of 0.049. QMG was measured in 2 out of 9 patients, with a pre- and post-treatment mean difference of -10.500, with a p-value of 0.258. 1 patient, with autoimmune myelopathy, didn't return to spontaneous breathing, nor to a good muscular function.

Conclusions
Despite the small sample size, DFP has shown clinical utility in the improvement of the muscular and respiratory function in patients with neurological autoimmune disorders.

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Day 2 - Transplantation: From Conservation to Organ Regeneration

In-situ Perfusion

A106

Donare Study Final Results – Randomized Research On In-Situ Adsorption Of Proinflammatory Mediators In Controlled DCD donors

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Introduction
Donation after cardiac death (DCD) can be an important source for expanding the numbers of organs suitable for transplantation. Italian peculiarities (20 minutes no-touch-period) in controlled DCD (cDCD) raise concern over organ ischemic damage, even performing Normothermic Regional Perfusion (NRP), highly recommended in all potential cDCD donors. DONARE study was designed as a randomized trial in 2019 to evaluate whether the insertion of a system capable of adsorbing inflammatory mediators during NRP leads to a reduction in cellular oxidative damage potentiality, assessed as a decrease in the levels of proinflammatory substances. This report describes the general final results.

Methods
The study protocol was defined by the DCD national working group and proposed to all the Italian DCD donation centers. The coordinating center (Italian National Transplant Center, CNT) has monitored the evolving cDCD activity to preserve the study capacity of representing the Italian scenario. Samples have been blindly centralized to an independent laboratory for cytokines profiling and information on the recovered organs has been provided by participating centers.

Results
The 40 planned cases were enrolled from September 2020 to March 2023 by 7 donation centers with randomization 1:1 in treatment with the adsorbent filter (CytoSorb) and Control group. No study-related adverse event has been reported. No significant differences in baseline characteristics were registered between the groups. The median donor age was 66.5years. Median NRP flow was 2.850 ml/min, decreasing over time (3.100 ml/min at t0, the beginning of NRP; 2.450 ml/min at the end of NRP), without affecting the CytoSorb flow in the treated group (268 (200-352.5) ml/min). NRP average duration was 190 ($\pm$44) minutes. Out of 40 enrolled cases 38(95%) became utilized donors. Hourly samplings were performed in all procedures for cytokines profiling. All analyzed cytokines (IL-6, IL-8, IL-10), except TNFa, expressed an increasing trend over time, on average with lower end values in CytoSorb group, showing a possible role in treatments in removal of target molecules, even with levels abnormeously higher than the reference serum levels.

Conclusion
The final evaluation for the DONARE study shows the safety and the feasibility of Apheresis integration in NRP for inflammatory mediator modulations in cDCD donors.

A107

Donare Study – Adsorption Of Inflammatory Mediators During In-Situ Normothermic Regional Perfusion In Controlled DCD Organ Donors

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Introduction

During all the steps of controlled DCD donation (cDCD), organ ischemia/reperfusion injury (IRI) is driven by production and accumulation of inflammatory mediators. In the Italian scenario, IRI can be exacerbated by the mandatory prolonged warm ischemia time associated to 20minutes of no touch period. A randomized study was performed to describe the inflammatory biomarkers (cytokines) trend during abdominal normothermic regional perfusion (NRP) in potential cDCD donors and the effect of an adsorbent filter included in the NRP circuit.

Methods

The study protocol was defined by the DCD national working group and proposed to all the Italian DCD donation centers, randomizing 40 donors in 1:1 ratio, with/without the adsorbent filter, hourly determining hemodynamic/metabolic parameters and laboratory data including blind cytokines dosage (IL-6, IL-8, IL-10, IL-1b, TNFa). The amount of cytokines (pg) adsorbed (Mass-Balance, filter inlet-outlet) was calculated.

Results

Despite a decrease of the NRP blood flow over time (3100ml/min at NRP-T0;2450ml/min at NRP-End), the CytoSorb© filter flow remained in the operational range (268 (200-352.5) ml/min). No differences resulted between the groups regarding lactates, pH, ALT, bilirubin, and creatinine. Ninety-five percent of the studied cases became utilized donors (93% and 88% livers, 47% and 73% kidneys, in the treated and control group, respectively). All cytokines, apart TNF-å, showed an increasing trend over time, lower in the CytoSorb© group, reaching extremely high levels if compared to the reference serum values (more than 500times for IL-6). On average, the CytoSorb© filter adsorbed 14705124.54pg of cytokines during NRP before organ recovery (3.3±0.9 hours, Fig. 1), in a concentration-dependent mode.

Adsorbed (pg)	MB IL-6	MB IL-8	MB IL-10	MB IL-1b	MB TNF-a
	8.116.941,64	1.661.684,59	2.795.689,19	3.436,78	2.127.372,34

$$Adsorbed = ((C_{pre})^{-}-(C_{post})^{-})_{\Delta t} * flow * \Delta t$$

C_{pre}/C_{post}= mean concentration of the target molecule between tx and tx+1 at CytoSorb Inflow/Outflow

Δt= Time duration between timepoints: tx and tx+1

Flow = Plasma Flow through CytoSorb = $Q_{CytoSorb} \times (1\text{-hematocrit})$

$Q_{CytoSorb}$= Blood Flow through CytoSorb

Figure 1 | Amount of Cytokines Adsorbed on average per treatment

Conclusion

CytoSorb© integration in cDCD donor NRP treatment is safe and potentially useful, removing high quantity of proinflammatory mediators. Larger experience is needed for establishing its routinely use in cDCD, even sequentially, during in-situ NRP and ex-situ organ perfusion and its impact on the organ outcome.

A108

Role Of Blood Lactate Levels In Kidney Suitability For Donation After Circulatory Death: A Retrospective Analysis

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Introduction

Donation after Circulatory Death (DCD) has emerged as a vital strategy to address organ shortages in transplantation. However, ischemia-reperfusion injury (IRI) remains a significant challenge, impacting organ viability and outcomes. This study explores the correlation between blood lactate levels during transplantation Normothermic Reperfusion (NrP) and kidney suitability for transplantation, aiming to identify potential biomarkers that could guide donor selection and organ assessment.

Methods

This retrospective analysis included 21 DCD kidney donors admitted to the ICU at Ospedale Civile di Baggiovara (Modena, Italy) between 2018 and 2019. Donor data collected included age, ICU admission diagnosis, noradrenaline administration, duration of ICU stay, blood lactate levels, and Karpinski scores evaluating organ suitability. Normothermic reperfusion was performed using ECMO and CytoSorb® hemadsorption. Lactate and creatinine levels were sampled at multiple time points during NrP (T0 to T3). Statistical analysis included univariate logistic regression and mixed models, with significance set at $p < 0.05$.

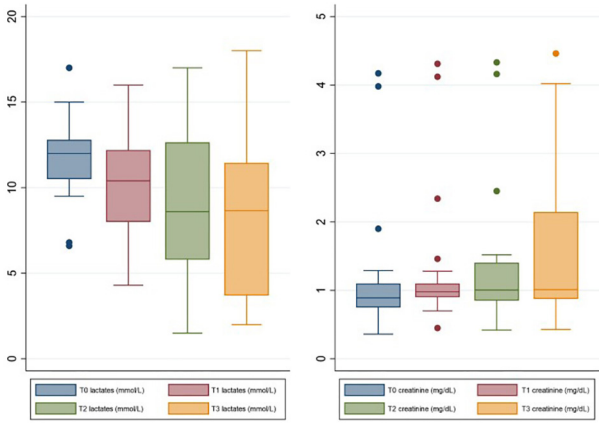

Figure 1 | Principal variations in lactate levels and plasma creatinine during NrP

Results

Lactate levels decreased significantly during NrP from T0 (11.89 ± 2.78 mmol/L) to T3 (8.19 ± 5.13 mmol/L, $p = 0.009$) (Figure 1). Initial T0 lactate levels correlated negatively with Karpinski scores, indicating that higher lactates may be associated with reduced organ damage and better transplantation suitability (OR 2.20; 95% CI 1.04–4.71; $p = 0.038$). Age also significantly predicted suitability (OR 0.69; 95% CI 0.51–0.93; $p = 0.016$) (Figure 1). Plasma creatinine levels increased during NrP but did not correlate with organ suitability.

Conclusion

This study suggests that higher initial lactate levels in DCD donors may not negatively affect organ suitability for transplantation, and a significant decrease during NrP may reflect better mitochondrial function and reduced IRI. Monitoring lactate trends could help assess organ viability and enhance transplantation success, although larger studies are needed to confirm these findings.

A109

First Application Of A Novel System For Hypothermic Temperature-Controlled Allograft Preservation In Heart Transplantation

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Introduction
Cold static graft preservation remains a cornerstone in both donation after brain death (DBD) and controlled donation after circulatory death (c-DCD) heart transplantation (HTx), particularly when in situ graft viability must be assessed via thoraco-abdominal normothermic regional perfusion (TA-NRP). We evaluated a novel temperature-controlled static cold storage system that offers real-time temperature and shock monitoring, GPS tracking, and Bluetooth connectivity. The system utilizes certified phase change materials (PCM) to maintain a consistent graft temperature between 4–8°C for up to 36 hours, avoiding direct ice contact and minimizing hypothermic injury, in accordance with international guidelines.

Methods
Nine donors (7 males, 2 females; mean age 41.3 ± 16.7 years) were accepted for transplantation, including two c-DCDs evaluated via TA-NRP. All grafts were preserved and transported using the novel system. Post-transplant assessments included clinical evaluation, laboratory biomarkers (NT-proBNP, lactate, CK-MB, troponin I), imaging (echocardiography), invasive hemodynamics (right heart catheterization), and histological analysis.

Results
Nine recipients (mean age 45.8 ± 16 years), including one re-transplant and five urgent listings, underwent HTx using grafts preserved with crystalloid cardioplegia and stored with the novel system. Mean cross-clamp and CPB times were 147.7 ± 41.3 and 160.9 ± 25.7 minutes, respectively. For DCD donors, mean functional warm ischemia time was 40.5 ± 6.4 minutes. CPB weaning was achieved with low-dose inotropes. No cases of severe primary graft dysfunction (PGD) requiring mechanical circulatory support occurred. Mean ventilation time was 21.9 ± 43.6 hours; ICU stay averaged 5.5 ± 7.7 days. Two patients required temporary renal replacement; one had prolonged ventilation. Cardiac biomarkers progressively normalized over 30 days. Echocardiography confirmed preserved biventricular function (LVEF >60%, RV FAC >25%) without significant valvular regurgitation. Right heart catheterization demonstrated stable hemodynamics; pre-implant biopsies ruled out edema. No 30-day mortality occurred.

Conclusions
Temperature-controlled static preservation appears safe and effective, with encouraging outcomes in terms of PGD prevention, hemodynamic stability, and early recovery. The system's usability and cost-effectiveness support broader clinical adoption. Larger multicenter studies are warranted to confirm its value in varied procurement scenarios.

A110

Endothelial And Inflammatory Responses During Normothermic Ex-Vivo Heart Perfusion In A Porcine Model

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Introduction

Heart transplantation is limited by donor scarcity, short cold storage (CS) and primary graft dysfunction (PGD). Normothermic ex vivo heart perfusion (NEVHP) offers extended preservation and reduced ischemia-reperfusion injury but is assessed mainly via lactate kinetics. Given NEVHP's artificial conditions and increasing marginal/DCD donor use, assessing endothelial and inflammatory responses as key PGD factors is highly relevant. We conducted a monocentric pilot study on five brain-dead donor hearts at Rennes University Hospital, revealing strong inflammation and endothelial activation. To explore these findings, we developed a translational porcine NEVHP model.

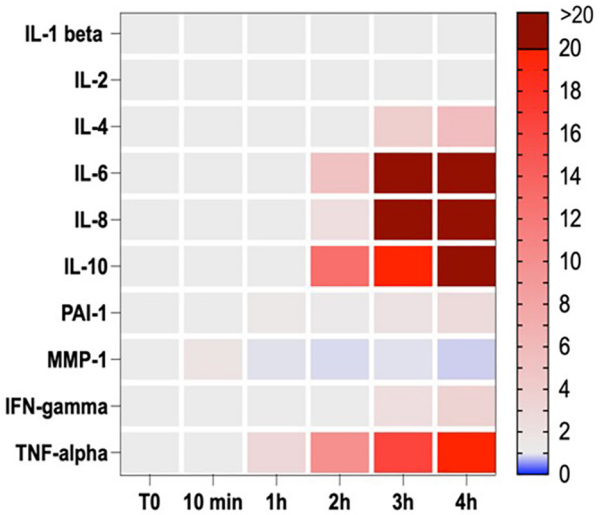
Methods

The study was conducted at INSERM U1241 and INRAE UE3P, following ethical guidelines. The procedure was integrated into a uterine transplantation model simulating multi-organ procurement. Beating-heart procurement was performed on post-pubertal Large White sows. After explantation hearts were stored in CS for 2 hours—mimicking regional transport time—followed by 4-hour NEVHP. The circuit was primed with 1200 ml donor blood, unfractionated heparin and a nutrient solution. Coronary flow was maintained between 650–850mL/min, and lactate levels were monitored per clinical and OCS guidelines. Perfusate samples were collected at baseline with only donor blood (T0), shortly after heart connection (T10), and hourly. Inflammatory cytokines were measured via Luminex®, and endothelial markers by ELISA.

Results

Seven procedures were completed. Myocardial resuscitation was confirmed, with average coronary flow of 710 ± 180.3 mL/min and a significant decrease in arterial lactate from T10 (4.45 [3.27–5.11] mmol/L) to T4h (2.12 [1.59–3.35] mmol/L). Sequential analysis of inflammatory and endothelial biomarkers revealed both pre-perfusion injury and perfusion-related changes (Figure 1).

A.



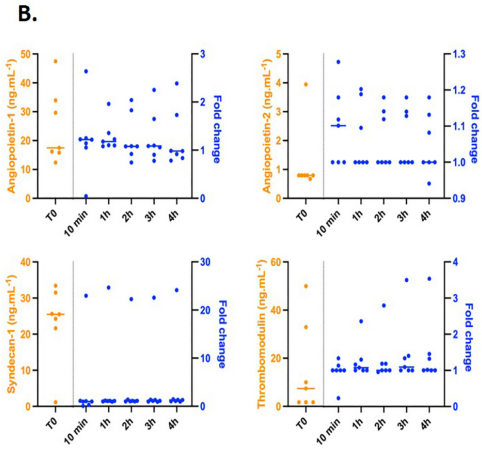


Figure 1 | **Evolution of biomarkers during normothermic ex-vivo heart perfusion. (A)** Inflammatory markers: results are expressed as fold changes relative to T0 (fold change = concentration at Tx / concentration at T0). **(B)** Endothelial markers: results at T0 are expressed as raw concentrations. Results at subsequent time points are expressed as fold changes relative to T0 (fold change = concentration at Tx / concentration at T0)

Conclusion

This is the first study to examine inflammatory and endothelial changes during porcine NEVHP. Despite limitations such as small sample size and hemodilution, it demonstrates the feasibility of dynamic biomarker monitoring. These findings provide insights to refine preservation protocols and improve future graft performance.

A111

Homemade System for Ex Vivo Perfusion of Porcine Heart Grafts from Beating Heart Donors Using a Pulsatile ECMO Console and a Repurposed OCS Kit

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Introduction

Heart transplantation is limited by donor scarcity, short cold storage times, and the risk of primary graft dysfunction (PGD)1. **Normothermic ex vivo heart perfusion** (NEVHP) offers a way **to reduce ischemia-reperfusion** injury, **extend preservation**, and include **marginal or DCD donors**. However, current graft evaluation mainly relies on lactate clearance, overlooking key biological responses. Artificial surfaces and non-physiological flow in NEVHP circuits can trigger inflammation and endothelial activation—both central to PGD. A pilot study at Rennes University Hospital using brain-dead porcine donors revealed significant inflammatory and endothelial responses during perfusion. To investigate these mechanisms further and develop a more accessible research platform, we built a translational porcine NEVHP model using a pulsatile ECMO (MEDOS) system and a repurposed OCS Heart kit.

Methods

Seven porcine hearts were retrieved following a beating-heart protocol. After 2 hours of cold storage, grafts were perfused for 4 hours using a **homemade NEVHP circuit** combining a **pulsatile MEDOS ECMO console** and a **repurposed OCS Heart kit**. The circuit was primed with autologous blood, heparin, and a nutrient solution (corticoids and vitamins). Perfusion followed clinical and OCS standards, maintaining **coronary flow at 650–850mL/min**. **Lactate levels** were collected at baseline, 10 minutes post-connection, and every 30 minutes.

Results

All perfusions were hemodynamically stable, with consistent myocardial reanimation confirmed by a mean coronary flow of 710±180mL/min. Arterial lactate levels significantly decreased from 4.45 [3.27–5.11] mmol/L at T10 to 2.12 [1.59–3.35] mmol/L at 4 hours, indicating effective metabolic recovery.

Conclusion

This low-cost, homemade ex vivo perfusion system combines a pulsatile MEDOS ECMO console with a repurposed OCS Heart kit to create a **clinically relevant** and **flexible platform** for porcine heart graft evaluation. Consistent coronary flow and a significant decrease in arterial lactate confirm **effective myocardial resuscitation**, validating the physiological robustness of this beating-heart model. The setup enables both functional and biological assessment under near-clinical conditions. Its affordability and reproducibility make it a valuable tool for translational research, perfusion strategy development, and surgical training—particularly in the context of marginal or DCD donor grafts.

A112

Efficacy Of Hemoadsorption Therapy In Post-Heart Transplant Hyperbilirubinemia Following End-Stage Non-Obstructive Hypertrophic Cardiomyopathy: A Case Series

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Introduction

Heart transplantation represents the definitive treatment for end-stage non-obstructive hypertrophic cardiomyopathy. However, the postoperative period is often complicated by hepatic dysfunction and metabolic alterations, including hyperbilirubinemia (up to 10%), which is associated with an in-hospital mortality rate exceeding 25% in recipients. The possible causes of hyperbilirubinemia include hepatic injury due to hypoperfusion, venous congestion due to graft dysfunction or sepsis as well as systemic inflammatory reactions triggered by the surgical procedure itself (e.g. cardiopulmonary bypass).

The timely adoption of extracorporeal supportive therapies such as continuous renal replacement therapy (CRRT) combined with CytoSorb can lead to a marked improvement in clinical parameters.

Methods

Two patients diagnosed with end-stage non-obstructive hypertrophic cardiomyopathy underwent orthotopic heart transplantation. In the postoperative period, both developed a significant increase in total and direct bilirubin levels, suggesting transient hepatic impairment caused by right heart graft transient dysfunction. To counteract this condition, CytoSorb was applied for 48 hours using two consecutive cartridges.

Results

The use of CytoSorb resulted in a significant reduction in total and direct bilirubin levels. An additional observed benefit was the reduction in creatine phosphokinase levels (CPK), suggesting an improvement in liver function and more efficient toxin elimination. The stabilization of hepatic parameters enabled more effective postoperative management, progressive organ function recovery, CRRT discontinuation, and patient discharge.

Conclusions

These two cases highlight the potential benefits of CytoSorb in managing post-heart transplant hyperbilirubinemia. The use of CytoSorb in these patients (Figure 1: patient 1 and 2) demonstrated efficacy not only in bilirubin reduction but also in lowering CPK levels, suggesting a positive effect on hepatic metabolism. The device's ability to remove bilirubin and both pro- and anti-inflammatory cytokines from the

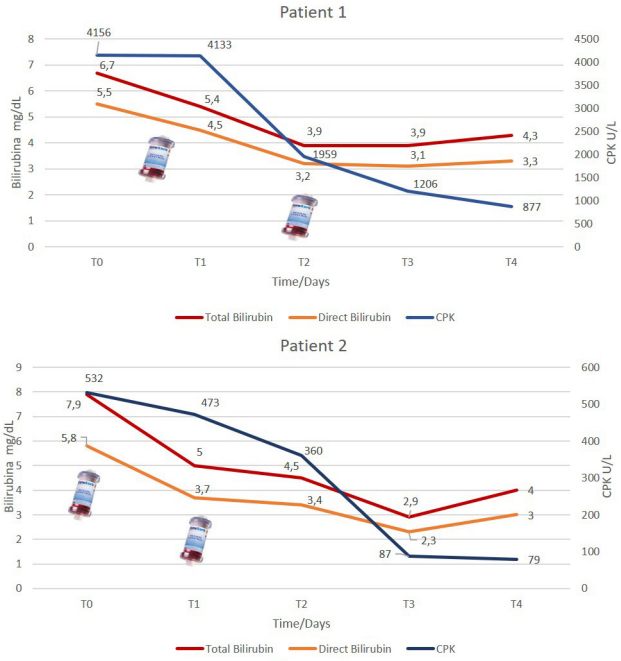

Figure 1 | Total Bilirubin, Direct Bilirubin and CPK trend over treatment period for patient 1 and patient 2

bloodstream may represent an effective therapeutic option to improve liver function and reduce the risk of post-transplant complications.

Lungs Transplantation

A113

Use Of Cytosorb Hemoperfusion In A Bilateral Lung Transplant Patient With Sepsis And Acute Kidney Injury: A Case Report

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Introduction

This case report describes a 65-year-old male who underwent bilateral lung transplantation for Idiopathic Pulmonary Fibrosis (IPF) with a Usual Interstitial Pneumonia (UIP) pattern associated with rheumatoid arthritis.

Methods

The patient, a former smoker, had a history of arterial hypertension. The transplant procedure was complicated by airway bleeding. Following the isolation of NDM-producing *Klebsiella* in the bronchoalveolar lavage, antibiotic therapy with ceftazidime/avibactam and aztreonam was initiated. Due to a high SOFA score and the presence of anuria with hyperkalemia, the patient was started on citrate-anticoagulated continuous veno-venous hemodialysis (CVVHD) combined with CytoSorb hemoperfusion for 24 hours.

Results

Laboratory data were collected prior to CytoSorb initiation and up to four days post-treatment (Figure 1A). The data showed a reduction in White Blood Cell (WBC) count and a slight decrease in C-reactive protein (CRP). In contrast, lactate and procalcitonin (PCT) levels remained stable after treatment. The vasoactive inotropic score (VIS) was used to objectively quantify the level of hemodynamic support required (Figure 1B). The graph shows an increase in VIS up to 24 hours post-treatment, followed by a decrease over the subsequent days. This trend suggests that the combination therapy including CytoSorb may have contributed to hemodynamic stabilization and a reduced need for vasopressors, likely through modulation of the inflammatory response in this critically ill post-transplant patient. No dose adjustments of antibiotic therapy were required during treatment, and no CytoSorb-related complications were observed.

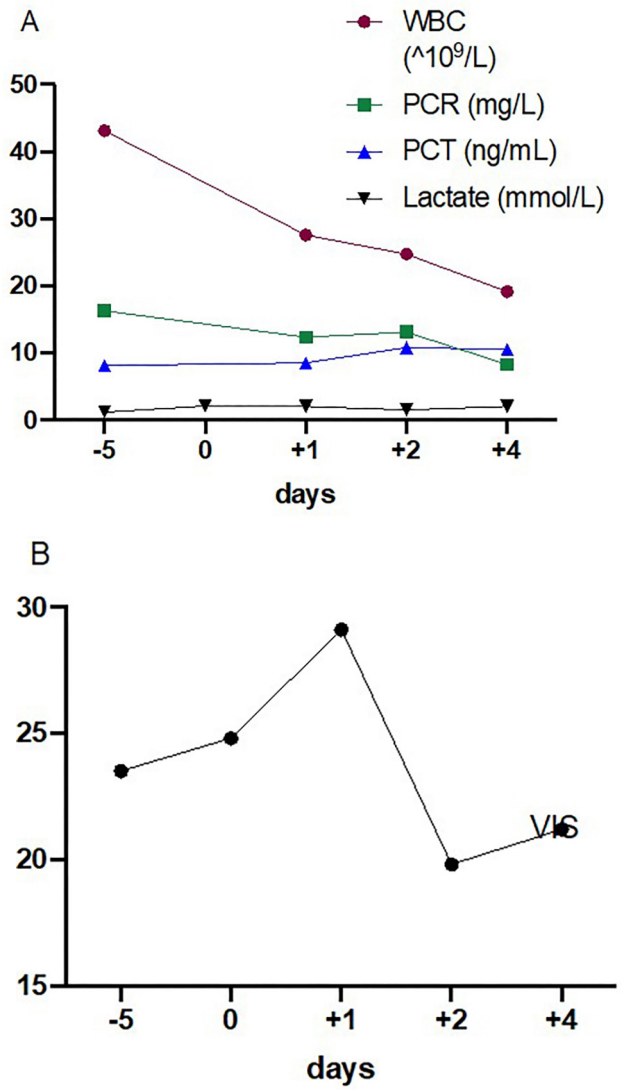

Figure 1 | Laboratory data and VIS score over treatment period

Conclusion

If these findings were confirmed in a larger patient population, and in light of existing literature, it could be suggested that the reduction in circulating catecholamines may help decrease vasoconstriction and reduce the risk of organ damage—highlighting CytoSorb potential in mitigating vasopressor-related toxicity.

A114

Application Of CytoSorb In Ex Vivo Lung Perfusion

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Introduction

Ex vivo lung perfusion (EVLP) is a transformative technique for assessing and rehabilitating donor lungs prior to transplantation. Despite its benefits, ischemia-reperfusion injury and inflammatory responses remain significant challenges, potentially compromising graft viability. CytoSorb®, a hemadsorption device engineered to remove inflammatory cytokines and mediators from blood or perfusate, offers a promising solution. Its integration into EVLP circuits may enhance lung preservation, attenuate inflammation, and improve post-transplant outcomes.

Methods

To mitigate inflammation during EVLP, a CytoSorb cartridge was integrated into the perfusion circuit (*Figure 1*). This setup facilitates the removal of pro-inflammatory mediators, aiming to stabilize metabolic parameters and enhance lung recovery, compliance, and gas exchange. The objective was to assess whether CytoSorb use leads to significant reductions in pro-inflammatory cytokines—specifically IL-6, IL-10, and MCP-1—and decreases the incidence of primary graft dysfunction (PGD).

Results

CytoSorb was utilized during three recent EVLP procedures prior to transplantation. All perfusions proceeded uneventfully, with no post-operative occurrences of PGD. Preliminary observations suggest feasibility and safety of CytoSorb integration. Analytical quantification of inflammatory mediator levels is ongoing and expected

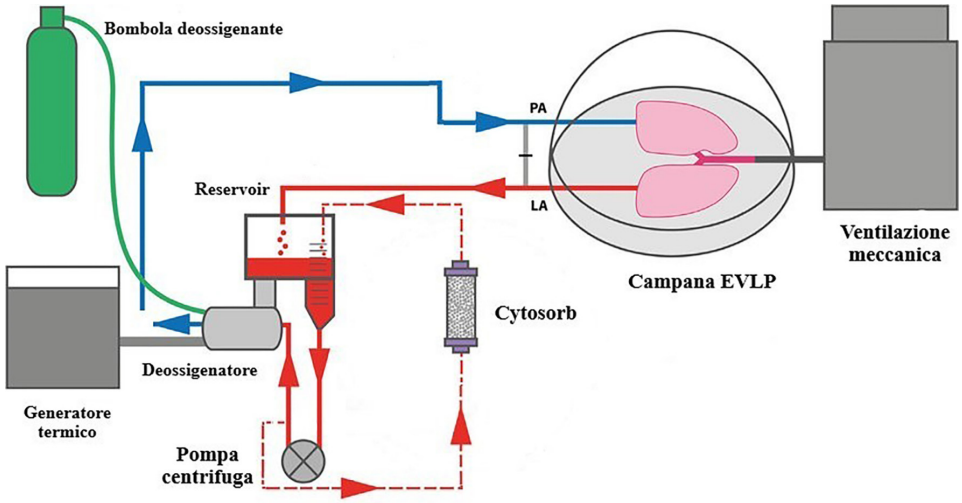

Figure 1 | Ex vivo lung perfusion circuit with CytoSorb integration

to further clarify its efficacy in reducing cytokine burden and improving graft quality.

Conclusion

CytoSorb use during EVLP appears to be a safe and viable approach to improve donor lung quality and transplant success. Its anti-inflammatory benefits may expand the pool of transplantable lungs and mitigate PGD risk.

Liver Transplantation

A115

Status Quo Of Need And Potential Role Of Machine Perfusion For Liver Transplantation In Germany

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Introduction

In Germany, donation after brain death (DBD) remains the sole source of organs. While potentially available, donation after circulatory death is not yet established and is unlikely to be implemented. Living donor liver transplantation (LDLT) also remains underrepresented.

Furthermore, the quality of DBD organs has declined: >60% are suboptimal (Donor Risk Index >1.5). Within the Eurotransplant region, particularly in Germany, the proportion of Extended Criteria Donor (ECD) livers now surpasses 50% and is projected to increase further. Concurrently, with the global rise in obesity, MASLD has become a significant concern in liver transplantation (LT) (~30% of post-mortem donations).

Several aspects of organ procurement introduce additional risks: limited qualification of procurement surgeons, inconsistent assessment, prolonged organ procurement times. The longstanding organ shipping system further exacerbates this, contributing to an extended cold ischemia time.

Collectively, these factors increase the marginality of grafts, leading to poorer outcomes and reduced survival rates after LT.

Methods

Traditional preservation methods, such as static cold storage (SCS), offer limited capacity to improve or assess the grafts. Unfortunately, SCS remains the predominant and often sole method of organ preservation in Germany. Machine perfusion (MP) represents a significant

advancement, offering the potential to optimize preservation and facilitate pre-transplant assessment. Despite the fact that most German transplant centers recognize MP as a crucial innovation and are either actively performing MP or about to start, practical experience in Germany is still relatively limited.

Results
Only 6/22 centers have performed more than 30 perfusions, with Hypothermic Oxygenated Machine Perfusion being the most frequently used procedure. A recent survey revealed:71% of low-volume centers perfuse all accepted organs; 83% of high-volume centers primarily perfuse marginal organs. An average 15% increase in utilization unanimously acknowledged a clear advantage of MP for German programs.

However, several obstacles hinder the routine implementation of MP in LT in Germany: the absence of dedicated studies and economic challenges, primarily because there is no reimbursement nor specialized personnel dedicated to MP.

Conclusion
The current critical situation, characterized by organ scarcity and declining organ quality, clearly underscores the urgent need for the standardized utilization of MP in LT.

A116

Liver Transplantation From Very Old DCD Donors: A Single Center Experience

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Introduction
The growing demand for organs, coupled with an aging general population, has led to increased consideration of elderly donors. While the use of very old donors is now widely accepted in the context of donation after brain death (DBD), such donors have often been excluded in donation after circulatory death (DCD). However, following positive outcomes in selected cases, there is growing interest in expanding the use of marginal DCD, particularly those of advanced age.

Methods
We report our experience with DCD-LT from donors >75 years, comparing results with those from donors <75 years. All DCD where Maastricht type III performed with normothermic regional perfusion adopting the PerLife system for ex-situ machine perfusion (MP with the following target parameters: Temperature (T) = 5–7°C; Pressures: Arterial (TAP) = 25-40 mmHg; Portal (TVP) = 4–6 mmHg. T, TAP, TVP, flows and resistances were continuously monitored.

Results
From November 2021 to December 2024, our center performed 38 DCD-LTs: 9 from donors >75 years and 29 from donors <75 years. The two groups were similar in terms of age, BMI, and cirrhosis severity (median age: 61 vs. 63 years, p = 0.34; BMI: 23.2 vs. 24.8, p = 0.21; MELD-Na: 17 vs. 16, p = 0.97). MP was used in 5/9 (56%) of DCD >75 and 17/29 (59%) of DCD <75. Functional warm ischemia time was similar (36 vs. 39 minutes), while cold ischemia time was longer in the <75 group (261 vs. 164 minutes, p = 0.42). One case of primary non-function occurred in the DCD <75 group. Early allograft dysfunction rates were similar (22.2% vs. 20.7%). The DCD <75 group had a higher peak ALT (579 vs. 436 U/L, p = 0.12) and a higher rate of acute kidney injury (31% vs. 11.1%, p = 0.23). The median follow-up was 17 (8–31 vs 3–48) months, biliary stricture rates were 11.1% vs. 20.7% (p = 0.46).

Conclusions
Our initial experience suggests that liver transplantation from elderly DCD (>75 years) yields acceptable results and is not inferior to standard DCD when appropriate patient selection and modern preservation technologies are used.

A117

The Role Of Machine Perfusion In DCD Donation: Marche Region Experience

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Introduction

Machine perfusion plays a crucial role in organ transplantation, particularly in Donation after Circulatory Death (DCD). DCD organs are vulnerable to ischemic injury due to warm ischemia time between circulatory arrest and organ retrieval. This technology enhances organ preservation, reduces ischemic damage, and improves post-transplant outcomes.

Methods

In Italy, the DCD procedure is meticulously structured to ensure ethical integrity, legal compliance, and optimal organ viability. Between 2024 and May 2025, 18 DCD cases were reported, with 17 confirmed at the liver transplant center of the Azienda Ospedaliero-Universitaria delle Marche in Ancona. All DCD livers underwent ex-situ machine perfusion using the PerLife® system (Aferetica Srl).

Results

Seventeen livers were perfused using Dual Hypothermic Oxygenated Perfusion (DHOPE). The mean perfusion duration was 106 minutes (min 33, max 847), at an average temperature of 7°C. Arterial (*Figure 1*) and portal vein flows increased during the procedure, indicating successful graft reconditioning. The median post-transplant peak AST was 1282 (range 144-6000), while ALT was 1104 (range 131-3300).

This approach reduces the ischemic injury of the grafts, improves preservation quality, and allows clinicians to monitor organ viability in real time. This method represents a significant improvement in the preservation of DCD livers, helping to reduce early allograft dysfunction and potentially expand the donor pool.

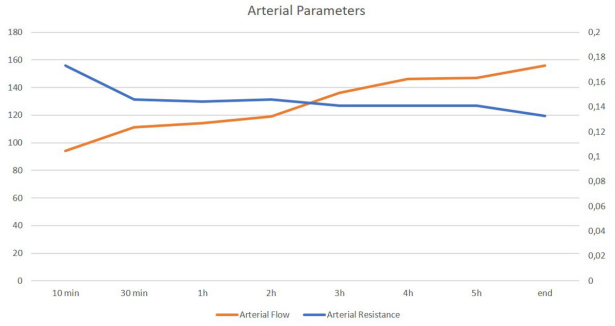

Figure 1 | Arterial perfusion parameters

Conclusion

Marginal organ donation is increasingly becoming standard practice in transplant programs. The combination of normothermic regional perfusion (NRP) and machine perfusion (MP) has become essential in DCD organ transplantation, contributing to the increased utilization of DCD organs across Italy. Machine perfusion technology is transforming DCD organ transplantation by enhancing preservation, reducing ischemic damage, and enabling real-time viability assessment. This technology not only helps recondition the grafts but also provides valuable information regarding organ viability before transplantation, ultimately improving transplant outcomes and expanding the donor pool.

A118

A Preliminary Experience With HOPE Ex-Situ Liver Treatment For Transplantation

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Introduction

Liver transplantation (LT) is a life-saving treatment. Ex-situ hypothermic oxygenated perfusion (HOPE) is an established treatment for liver graft preservation and recovery for transplantation. Although we have proven experience in normothermic ex-situ perfusion (NMP), we decided to explore the potentials of HOPE in extended criteria donor (ECD) liver perfusion, as it is considered a safe and efficient technique with excellent long-term outcomes. Here we report 2 cases of HOPE performed in our center.

Methods

2 liver grafts were recovered from extended criteria donors, one 76-year-old female donor with intracranial haemorrhage and one 60-year-old male donor with hypoxic brain injury after resuscitation and diabetes as well as hypertension and coronary heart disease in his medical history. After a backtable preparation and portal cannulation, each graft was connected to PerLife perfusion system (Aferetica, Bologna, Italy) to perform HOPE with the following target parameters: temperature (T) = 4°C; portal pressure (PP) = 10 mmHg; pure oxygen flow = 1 L/min. Portal flow (PF) and resistances (PR) were recorded every 5 minutes, from the treatment start (t_{start}) until the treatment end (t_{end}).

Results

The average treatment duration was 132,5 minutes (Case 1: 105 minutes; Case 2: 160 minutes). Between t_{start} and t_{end}, PF increased (Figure 1). The average T was 4,8±1,1°C). Both grafts were transplanted with uneventful post-operative course. Both patients were in intensive care unit for 1 and 2 days respectively and could be discharged after 7 and 12 days. To date both recipients show a normal graft function and are in a very good general condition (Follow up 9 and 6 months).

Case #	Case 1		Case 2	
Timepoints	t_{start}	t_{end}	t_{start}	t_{end}
PF (ml/min)	384	511	191	436
PR (mmHg/ml/min)	0,007	0,001	0,038	0,018

Figure 1 | Perfusion Dynamics

Conclusions

HOPE perfusion was safe and feasible. The results of our preliminary experience are consistent with already available evidence on this technique application in LT. This preliminary experience provides the groundwork for a routine clinical application of HOPE in our center.

A119

Hypothermic Oxygenated Perfusion In Liver Transplantation For Hepatocellular Carcinoma Patients With A Metroticket Lower Than 50%

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Introduction

Liver transplantation (LT) is the curative treatment in early stages of hepatocellular carcinoma (HCC), also treating the underlying liver disease. Individualized prognosis delivered by scores such as the Metroticket score, help sharing decision-making between clinicians. Hypothermic oxygenated perfusion (HOPE) methods have demonstrated protective results in HCC patients transplanted with perfused grafts.

Hypothermic Oxygenated Perfusion And Liver Transplantation For Hepatocellular Carcinoma: Lower Hepatic Recurrence And Increased Use Of Elderly Donors

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Introduction
Tumor recurrence after liver transplant (LT) has been associated with several factors, including ischemia-reperfusion injury (IRI). Hypothermic oxygenated perfusion (HOPE) reduces IRI and downstream inflammation. Studies suggest a decreased recurrence rate of hepatocellular carcinoma (HCC) in grafts undergoing HOPE. Our aim was to study tumor recurrence in HCC transplanted patients with grafts perfused with HOPE.

Methods
Retrospective analysis of 2 groups of HCC adult patients submitted to orthotopic LT between 08/2020 and 10/2023: not perfused and perfused with HOPE (according to the protocol, through portal vein for a minimum of 120 minutes). 100% brain dead donors.

Results
76 HCC patients were transplanted during the study period.

Methods
Retrospective analysis of 2 groups of HCC adult patients submitted to orthotopic LT between 08/2020 and 10/2023: perfused and non-perfused with HOPE (according to the protocol, through portal vein for a minimum of 120 minutes). 100% brain dead donors.

Results
76 HCC patients were transplanted during the study period, 24 not perfused with HOPE and 52 perfused with HOPE.

There was no difference in gender, age, MELD Na score or tumor burden. Donor's median age was significantly higher in the HOPE group (73 vs 58.5, p<0.001). Median Metroticket results (Lancet Oncology 2009) were also comparable between groups (p=0.067); HOPE group had 23.1% of patients with a Metroticket <50% vs 12.5%, although without statistical significance (p=0.282).

In patients with a Metroticket <50%, 2 patients died in the HOPE group (16.7%), deaths unrelated to tumor recurrence, vs 1 patient (33.3%) in the non-perfused group (p=0.519), who died do to disease progression with liver recurrence. 2-year overall survival was 90.9% vs 50% months (p=0.190). There was one recurrence in each group (8.3% vs 33.3%, p=0.255), with a 2-year disease free survival of 91.7% and 66.7%, respectively (p=0.307).

Conclusions
Despite the small sample size in both groups, HCC patients with a Metroticket <50% transplanted with grafts perfused with HOPE, appear to have longer.

Overall and disease-free survivals at 2 years, according to our results. However, further and larger studies are needed.

Not perfused group: 24 patients, median age 61 years (IQR 56-66). Donors' age 58.5 years (IQR 54.25-67.75) (0% ≥80years old). Cold ischemia time (CIT) 283.5 minutes (IQR 241.75-336.25). Follow-up of 45 months (IQR 22-50.75) with recurrence in two patients (8.3%), including hepatic recurrence. DFS of 95.8% at one year. At date of analysis, both patients with recurrence died (100%) due to disease progression.

HOPE group: 52 patients, median age of 62 years (IQR 56.25-66.75). Donors´ age 73 years (IQR 68.25-79) (23.1% ≥80years old). CIT 220.5 minutes (IQR 185.5-255), HOPE time 132.5 minutes (IQR 123-173.5). Reduced IRI severity (p=0.001). Follow-up of 29.50 months (IQR 23.25-37), with recurrence in four patients (7.7%), only extrahepatic. DFS of 98% at one year. There was no mortality in patients with recurrence in this group.

Recurrence rate (p=1.000) and DFS (p=0.913) were similar between groups, but patient didn't have hepatic recurrences in the HOPE group. In the HOPE group 23.1% of patients had a Metroticket result ≤50% and only one of these had HCC recurrence. There was a significant difference in donors' age (p<0.001), as well as in CIT (p<0.001).

Conclusions
In our Center, the use of HOPE appears to reduce hepatic recurrence after LT for HCC and the consequent mortality. It allowed the use of grafts from donors aged ≥80 years old, improving access to LT for these patients, and significantly reduced the CIT and IRI severity.

A121

From Rescue Technique To Optimization Strategy: The Role Of Hypothermic Oxygenated Perfusion In Good-Quality Livers – A Single-Center Experience

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Introduction
The introduction of liver perfusion techniques has been a major milestone in liver transplantation (LT) over the past decade. Several studies have shown that hypothermic oxygenated perfusion (HOPE) improves post-transplant outcomes when using extended criteria donors (ECD). Our center has been using HOPE since 2020 and, from 2024 onwards, the technique has been applied to all grafts. The aim of this study is to evaluate the impact of HOPE on LTs performed with non-ECD grafts.

Methods
We conducted a retrospective analysis of LTs performed between 19/08/2020 and 30/11/2024. Donors were excluded if they met any of the following criteria: age>67 years, BMI>30 kg/m^2, cold ischemia time (CIT)>8 hours, macrosteatosis>30%, serum sodium >165 mEq/L, ALT>3× upper limit of normal, ventilation >7 days. Two groups were defined: HOPE and NO HOPE, with follow-up >6 months. For the assessment of ischemic-type biliary lesions (ITBL), cases with post-transplant hepatic artery thrombosis or stenosis, or with primary sclerosing cholangitis, were excluded.

Results
A total of 100 LTs were included: 43 in the HOPE group and 47 in the NO HOPE group. All donors were after brain death. In the HOPE group, median CIT was 240 minutes (IQR:204–271), HOPE duration 135 minutes (IQR:126–160), and peak ALT 431.5 U/L (IQR: 218.75–1076.75). Median follow-up was 450 days (IQR:270.5–963.25), with a mortality rate of 9.3% and no cases of re-transplantation. In the NO HOPE group, CIT was 300 minutes (IQR:259–340), peak ALT 597.5 U/L (IQR:392.25–1341.75), and follow-up 982.5 days (IQR:579.75–1375.25); mortality was 19% (including one ITBL-related case), and re-transplantation rate was 3.5%. The incidence of ITBL was significantly lower (p=0.024) in the HOPE group (2.9%, 1/34 *vs.* 15.6%, 7/45). No other significant differences were observed.

Conclusion
In our center, the use of HOPE in non-ECD grafts was associated with improved post-LT outcomes, with a significant reduction in the incidence of ITBL. Additionally, HOPE may have contributed to the lower mortality observed in this group.

A122

Divide And Preserve: Hypothermic Oxygenated Perfusion In The Context Of Liver Split

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Introduction
Hypothermic oxygenated perfusion (HOPE) has been shown to mitigate ischaemia-reperfusion injury (IRI), which is associated with poorer outcomes in liver transplantation (LT), particularly in split liver grafts that are more susceptible to IRI.

We aim to present the application of hypothermic oxygenated perfusion (HOPE) during liver split procedures, demonstrating the feasibility of simultaneous perfusion of both liver lobes.

Methods
We report two clinical cases in which HOPE was applied during the liver split procedure, enabling simultaneous perfusion of both lobes until the end of the surgery. The portal vein was cannulated early, allowing prompt initiation of oxygenated perfusion. The split was performed using standard technique, with division of the right branch of the portal vein as the final step, thus maximizing HOPE duration.

Results
Case 1 – 08/03/2025; Adult recipient: Preservation time (PT): 606 minutes; cold ischemia time (CIT): 237 minutes; HOPE time (HT): 369 minutes; Peak ALT: 2264 U/L. Pediatric recipient: PT: 380 minutes; CIT: 198 minutes; HT: 120 minutes; Peak ALT: 1258 U/L. Intraoperatively, both recipients developed hepatic artery thrombosis, managed with fibrinolytic therapy.

Case 2 – 12/04/2025; Adult recipient: PT: 594 minutes; CIT: 232 minutes; HT: 362 minutes; Peak ALT: 619 U/L. Pediatric recipient: PT: 504 minutes; CIT: 324 minutes; HT: 180 minutes; Peak ALT: 553 U/L.

Follow-up until 20/06/2025: no complications in adult recipients; one pediatric recipient developed antibody-mediated rejection within the first post-LT month.

Conclusion
Simultaneous HOPE of both lobes in split LT is feasible using a single perfusion kit. This strategy allows to reduce CIT and may contribute to lower post-LT hepatocellular injury. Further follow-up is required to assess mid- and long-term outcomes.

A123

Split Liver In HOPE – A Preliminary Experience

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Introduction
Hypothermic Oxygenated Ex-Situ Perfusion (HOPE) has emerged as an effective strategy to improve outcomes in marginal whole liver grafts by mitigating ischemia-reperfusion injury, reducing cold ischemia time (CIT), and safely extending preservation time. Split liver (SL) transplantation represents a valuable technique to increase the availability of size-matched grafts, particularly for paediatric recipients. The integration of machine perfusion (MP) technology in SL procedures holds promise for further optimizing organ utilization by enabling extended criteria donor use, offering a controlled environment for technically demanding procedures and addressing logistical challenges in transplantation. We aimed to analyze our preliminary experience with SL during HOPE.

Methods
We retrospectively analyzed our experience with four SL procedures performed during end-ischemic HOPE using the PerLiver® system (Aferetica, Italy). HOPE parameters were adapted from the standard protocol for whole liver perfusion.

Results
From September 2023 to June 2025, four SL procedures were performed: two full left/full right SL, one hyper-reduction of a left lateral segment, and one conventional SL. Donor grafts were procured in demanding clinical contexts, such as hemodynamic instability of the donor, difficult logistics and technically complex procedures. The median total preservation time was 599 minutes (IQR 532–683), with a median HOPE duration of 194 minutes (IQR 97–247) and a median CIT of 434 minutes (IQR 382–459). The completion rate of the SL procedures was 100%, and no adverse events were observed during HOPE. All grafts were successfully transplanted, with no cases requiring re-transplantation. At the time of reporting, all recipients are alive and well.

Conclusion
This is a preliminary report on SL during HOPE, showing the safety and feasibility of the procedure. Further, larger studies are needed to confirm these results and guide the use of machine perfusion in SL transplantation.

A124

Ex-Vivo Hypothermic Oxygenated Perfusion And Cytokine Filtration (Cyto-HOPE) Of Human Liver Grafts: A Randomized Controlled Trial

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Hypothermic Ice-Free Conditions For Static Cold Storage Of Livers For Transplantation: A Case Series

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Introduction

The traditional technique for donor liver preservation during transport (LPT) is static cold storage (SCS) using an icebox and a three-bag layer around the graft. It is a simple and inexpensive solution, but it has some limitations: non-standardized organ conditions, particularly non-homogeneous thermal conditions, increased risk of freezing injury, and no organ traceability during transport. Over the past decade, technological evolution has led to the introduction of new preservation systems with the aim of improving the quality of this step in the transplant process. In this report, we present a case series of LPT using a new hypothermic SCS technology, the PerTravel system, which allows for 2-6°C ice-free hypothermia, as well as continuous real-time monitoring of localization and LPT stability.

Methods

Between March and June 2025, three LPT procedures were performed with PerTravel in an airplane. Organ preparation was carried out according to our standard techniques. A three-bag set and a solid organ container were used with standard SCS liquid. The PerTravel LPT mission allowed continuous and real-time monitoring of organ and environmental temperature, localization and stability.

Results

The maximum transport duration was 4 hours. The average recorded organ temperature was 6°C, and the average environmental temperature was 22°C-26°C. No LPT-associated adverse events were reported.

Conclusion

This case series is a preliminary report suggesting the feasibility and safety of LPT with a new hypothermic SCS technology, demonstrating stable organ conditions during the process. Further studies are needed to deeply explore the clinical impacts and benefits of standardizing conditions in LPT.

A126

Real Life Experience On Organ Transport With PerTravel®: Continuous Temperature And GPS Tracking Without Ice

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Introduction

The traditional method for transporting liver graft involves static cold storage (SCS) using water and ice to cool and preserve the liver within a triple-layer of bags. Although this technique is simple and widely used, it has several limitations: inability to precisely control temperature, thermal heterogeneity, risk of freezing injury, and lack of traceability during transport.

PerTravel, an innovative hypothermic organ transport system, maintains a stable temperature between 2 and 6 °C for up to 36 hours without ice, employing phase change material (PCM) plate. This device can also monitor in real time both the temperature of the organ and surrounding environment, as well as the GPS location of the container, ensuring full control and continuous traceability throughout the logistic process.

Methods

Between March and May 2025, five livers from extended criteria donors were harvested and transported using the PerTravel system on dedicated vehicles. Organs were prepared for transportation following the standard protocol, including a triple layer of bags and a rigid container filled with preservation solution.

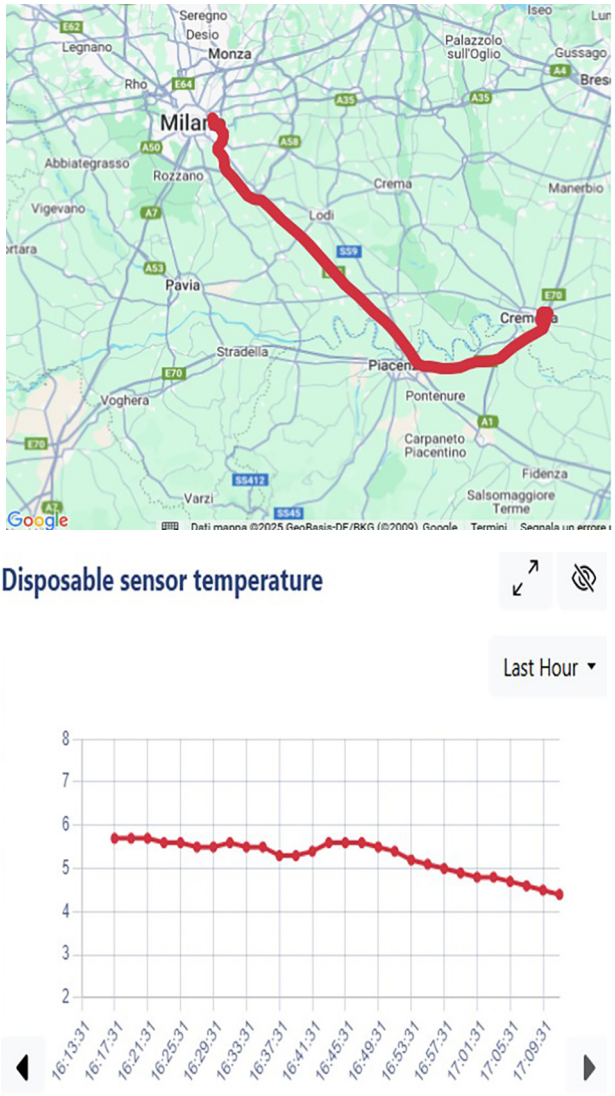

Figure 1 | Transportation monitoring

During each transport, real-time data on organ temperature, environment temperature, and device location were recorded continuously (Figure 1).

Results

The longest transport duration was 1 hour and 47 minutes. The mean organ temperature recorded was 7.53 °C, with an average preservation solution temperature of 8.2 °C, while ambient temperature ranged between 22.7 °C and 26.8 °C. No adverse events were reported. All grafts were implanted without graft-related complications.

Conclusion

The data from this first real-life application demonstrate that PerTravel is a safe, effective, and highly innovative system for organ transport.

The device maintained stable temperatures of the preservation solution -and consequently of the organ-even when the initial temperature of the solution was not ideally around 4 °C in some cases. The absence of ice, thermal stability, and continuous real-time monitoring represent a significant advancement in transplant logistics.

A127

Optimizing Liver Perfusion And Vascular Access During Machine Perfusion With Perlife®

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Introduction

Machine perfusion is revolutionizing the liver transplant panorama, offering new opportunities to enhance transplant quality and safety. Compared to static cold storage, dynamic perfusion reduces ischemia-reperfusion injury, improves cellular metabolism, facilitates toxin clearance, and allows pre-transplant functional assessment. In particular, ex situ hypothermic oxygenated perfusion (HOPE) has demonstrated significant benefits in preserving marginal or complex livers.

Methods

Thanks to the PerLife device developed by Aferetica, the liver is positioned in an organ chamber that is easily accessible, fully visible, and not submerged in perfusate.

In this approach, initially, it is separated the hepatic artery and portal vein from connective tissue and the inferior vena cava.

Perfusion is initially started via the portal vein, enabling early organ stabilization.

Dissection and preparation of the portal vein then continue up to the hepatic hilum. Once portal vein preparation is completed, dissection of the artery is initiated at the level of the celiac trunk, allowing initiation of dual perfusion (DHOPE).

This design provides optimal anatomical exposure, allowing the surgeon to perform hepatic artery reconstruction in cases of anatomical variants or complex vascular architecture, allowing control of leaks. Preparation of the liver graft ends with dissection and preparation of the retrohepatic vena cava and supra-hepatic veins.

Results

This operative strategy has shown a significant reduction in cold ischemia time, as the organ remains perfused from the early stages of preparation. Moreover, the ability to perform real-time arterial reconstruction improves graft suitability and reduces the risk of post-transplant thrombosis or malperfusion. Adoption of machine perfusion has also led to a higher utilization rate of organs previously considered marginal and successfully transplanted.

Conclusion

Machine perfusion, combined with direct and continuous access to the organ during treatment, represents a significant advancement in transplant medicine. The HOPE technique, initiated via the portal vein, followed by DHOPE after arterial preparation, not only reduces ischemic injury but also optimizes organ preparation. Notably, PerLife stands out for its design, which keeps the liver visible and not submerged in perfusate, providing the surgeon with excellent exposure to perform vascular reconstruction directly during perfusion, enhancing both precision and timing of the procedure.

A128

Role Of Machine Perfusion On Oncological Outcome In HCC Transplantation

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Introduction

Perfusion machines play a growing role in the field of liver transplants, improving the outcomes of organs harvested from donors with extended criteria (ECD), and in particular hypothermic perfusion (D-HOPE) allows the reduction of the risk of ischemic cholangiopathy, particularly in grafts taken from DCD. Little is still known about the impact of machine perfusion on the oncological outcome in terms of survival (OS) and oncological recurrence (DFS) of transplantation for HCC.

Methods

Retrospective analysis on a cohort of 243 consecutive patients undergoing LT for HCC at our center with donors ECD score =>2 subjected or not to hypothermic machine perfusion in the period 2019-2024.

Results

243 patients with grafts from DCD donors or with ECD Score > 2 underwent LT for HCC. 53 patients underwent D-HOPE. No significant differences were recorded in terms of etiology (Alcohol 22.7 Vs Viral 34.3 Vs Others 25.6 months p.176) strategy (Primary 31.4 Vs Downstaging 29.2 Vs Salvage 27.7 months p.853) or selective listing criteria (Milan Criteria IN 31.5 Vs OUT 25.63 months p.512) After a median follow-up of 42 months (range, 1 – 72) there were 12 deaths and 15 relapses. There were no significant differences in terms of OS and DFS. The 1-, 3- and 5-year OS is 93.9%, 88.9%, 80.6% respectively, while the DFS is 94.8%, 87.2%, 83.1%.

Conclusion

Initial analysis of this cohort suggests that machine perfusion does not appear to have a negative impact on oncological outcome while allowing the use of marginal grafts.

A129

Real-Time Evaluation Of Hepatic Perfusion Using Indocyanine Green Fluorescence Imaging In Hypothermic Machine Perfusion

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Introduction

Assessment of liver perfusion is a critical step in the pre-implantation phase of liver transplantation, particularly when the graft has undergone machine perfusion—either normothermic or hypothermic. In this context, indocyanine green (ICG) serves as a valuable non-invasive diagnostic tool for real-time monitoring of tissue perfusion and hepatic function. ICG is a fluorescent dye with high affinity for plasma proteins, rapidly taken up by hepatocytes and excreted into bile without undergoing metabolism. Its near-infrared fluorescence properties enable real-time visualization of intrahepatic vascular distribution, aiding evaluation of graft viability, especially in marginal organs.

Methods

Seven human livers (5 DCD, 2 ECMO DBD) were evaluated using hypothermic oxygenated machine perfusion (DHOPE). Upon completion of the perfusion protocol, each liver was injected with 25 mg of ICG via the portal vein and hepatic artery. A near-infrared imaging system

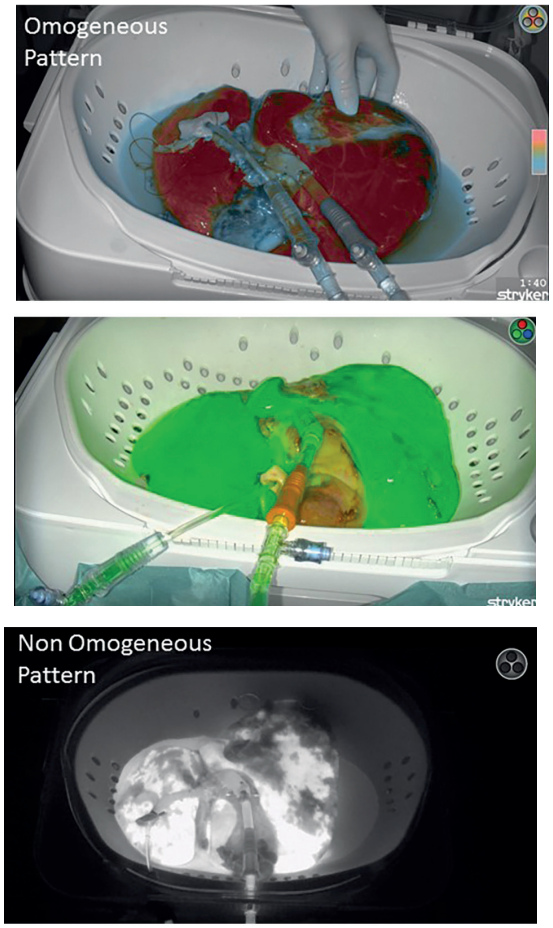

Figure 1 |

assessed fluorescence distribution and vascular homogeneity across the hepatic parenchyma. The pattern and intensity of fluorescence were documented and analyzed semi-quantitatively.

Results

Seven grafts from extended criteria donors (5 DCD, 2 ECMO DBD) underwent DHOPE for an average of 140 minutes (range 120–186) and were assessed with pre-implantation ICG-NIR imaging. Early homogeneous distribution of the tracer was observed in 4 cases. The total ischemia duration was similar between groups. A non-homogeneous fluorescence pattern was associated with post-reperfusion syndrome, higher lactate peak (8.2 vs 4.7), elevated cytolytic enzymes (average 2295, range 1355–3057 vs 534, 197–989), and prolonged hospital stay (average 20 vs 12 days). No adverse events related to ICG were reported (Figure 1).

Conclusions

ICG fluorescence imaging is a feasible and informative tool for evaluating hepatic perfusion in hypothermic machine-perfused grafts. It enables real-time assessment of intrahepatic vascular distribution and may help identify grafts at risk of primary non-function. This technique could complement conventional perfusion markers in transplantation decision-making.

A130

Prolonged Preservation Of Livers Donated After Circulatory Death Using Dual Hypothermic Oxygenated Machine Perfusion

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Introduction

Liver transplantation with grafts donated after circulatory death (DCD) increases the risk of early graft failure due to ischemia-reperfusion (IR) injury-related complications. A 2-hour period of dual hypothermic oxygenated machine perfusion (DHOPE) has been shown to reduce IR injury-related complications, especially non-anastomotic biliary strictures (NAS). While prolonged DHOPE may safely extend the preservation time for brain-dead donor livers, its safety in DCD livers remains unclear. This study evaluates the safety and outcomes of prolonged DHOPE in DCD liver transplantation.

Methods

Between June 2022 and August 2024, 22 DCD livers underwent prolonged DHOPE (≥4 hours), with a median follow-up of 8 months post-transplant. A 1:1 time-matched control DCD group underwent DHOPE <4 hours. Outcomes included the 7-day peak value of alanine-aminotransferase (ALT; U/L), international normal-

ized ratio (INR), and total bilirubin (µmol/L), as well as graft loss due to primary non function (PNF) or early hepatic artery thrombosis (eHAT) within 2 months. Death-censored graft survival and NAS incidence were assessed at 6 months. Data are presented as medians and ranges.

Results

The total preservation time was 12.0 hours (9.0-23.9) in the prolonged group and 8.8 hours (5.7-10.7) in the controls (p<0.001), with a respective DHOPE duration of 6.4 hours (4.7-19.7) and 3.0 hours (1.3-4.0). Peak laboratory values were comparable between groups: ALT (1525 U/L (440–3997) vs 962 U/L (335–4059), p=0.132), INR (2.2 (1.6–4.3) vs 2.4 (1.3–4.7), p=0.37), and bilirubin (108 µmol/L (23–282) vs 71 µmol/L (9–421), p=0.37).

Death-censored graft survival was not significantly different (86% vs 100%, p=0.23), although in the prolonged group, three patients required re-transplantation due to one case of PNF (5%) and two after eHAT (9%). Symptomatic NAS occurred in two patients in the prolonged group (9%) and none of the controls.

Conclusions

Prolonged DHOPE in DCD livers did not result in a significant increase in graft-related complications, including PNF, eHAT and NAS. While graft survival has to be monitored in longer follow-up, it now appears to be safe to extend DCD liver graft preservation. This approach can optimize transplant logistics and facilitate daytime surgeries for high-risk DCD liver recipients.

A131

Acute Kidney Injury Post Liver Transplant With Grafts Treated By Hypothermic Machine Perfusion

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Introduction

Many advantages were reported using the machine perfusion (MP) to rescue marginal grafts in the immediate- and long-term outcome. Acute kidney injury (AKI) is a common post-transplant complication using these livers that might compromise patient outcome and amplify the transplant cost.

Aim of the study was to analyze the immediate post operative outcomes, including the AKI between patients with MP graft (MP) versus recipients of graft cold stored (noMP), before and after a propensity score matching (PSM).

Methods

From a prospectively maintained database (January 2022 – September 2024), liver recipients in MP group versus noMP were compared. PSM was performed for donor risk index (DRI), macro-steatosis (MaS) > or <30% and recipient MELD, 3:1 (MP vs noMP).

Results

Of 129 transplants, 23 MP versus 122 noMP were compared. DRI (2 vs. 1.9, p=0.049), donor age (75 vs 66, p=0.01) and presence of moderate macro-steatosis (13% versus 2%) were higher in MP group versus noMP. Post operatively MP patients had a higher AKI but not statistically significant (57% versus 39%, p=0.86) and similar rate of stage 3 of AKI (13%vs13%) (Figure 1). After PSM, 23 MP were compared with 68 noMP (Figure 1). MP patients had grafts from higher donor age (75 versus 67, p=0.04),

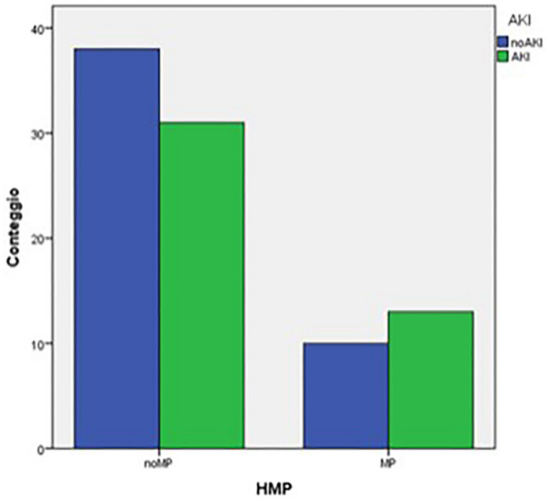

Figure 1 | AKI rates

better post operative liver function test and EAD but still high AKI (57% versus 44%, p=0.05). In PSM set, no one needed CVVH/dialysis and both groups were treated with the same immunosuppression protocol. Multivariate analysis showed the recipient pre-transplant creatinine level as the only significant risk factor for AKI (CI:1.84-43.48, OR:9, p=0.011). MaS>30% nearly reached the significant level (p=0.057).

Conclusion
MP remains an important device to rescue marginal livers. In the era of marginal grafts where all efforts aim to increase the donor pool, more post-operative attention should be given to preserve the renal function, even if HMP is used.

A132

Liver Transplants With Grafts With Moderate Macro-Vesicular Steatosis

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Introduction
In the era of machine perfusion (MP), macro-vesicular steatosis greater than 30% remains a significant risk factor that frequently restricts the utilization of liver grafts.

Methods
Four grafts with 45-50% steatosis were used, treated with end-ischemic DHOPE. The first two were connected to the Persorb filter, the first (A) for 290 minutes and the second (B) for 150 minutes. Compatibility and anthropometric characteristics were considered for matching.

Results
Graft A came from a 66-year-old donor, BMI 52, donor risk index (DRI) of 2.01, and approximately 10 hours of total CIT; Recipient A was a 66-year-old transplant recipient for ALD, HBV, and HCV-related cirrhosis, with MELD 12 and grade I portal vein thrombosis according to Yerdel. Patient A was extubated on the operating table, admitted directly to the sub-intensive care unit, and discharged after 13 days, without any surgical complications. Graft B came from a 64-year-old donor with a BMI of 64, a DRI of 2.05, DMID, and a 10-hour total CIT. Recipient B, a 68-year-old with HBV-HDV-related cirrhosis with MELD 16, had no complications other than a re-laparotomy for bleeding. Both recipients suffered AKI but were discharged with normal liver and kidney function.

Grafts C and D, perfused in HMP without Persorb, came from donors aged 44 and 49, respectively, with BMIs of 28 and 41, DRIs of 1.06 and 1.3, both undergoing approximately 10 hours of total cold ischemia. They were implanted in recipients aged 63 and 60, respectively, with ALD/MASH/HCV and HCV cirrhosis, with MELDs of 11 and 30. Recipient D underwent a combined liver-kidney transplant, with EAD for the liver graft and DGF for the renal graft but was discharged with normal function in both organs.

Conclusion
The combined treatment of HMP and the Persorb cytokine filter appears to be a viable strategy for grafts with moderate steatosis. Post-transplant renal function should be monitored, as these livers come from marginal donors.

A133

Dual Hypothermic Oxygenated Perfusion In Liver Transplantation: 2-years Single Center Experience

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Harnessing The Beneficial Effects Of Mesenchymal Stem Cells During Liver Machine Perfusion: Feasibility Of An Advanced Perfusion System Coupled With A Bioreactor

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Introduction
Dual hypothermic oxygenated machine perfusion (DHOPE) represents an established strategy to optimize liver grafts preservation, which have already showed both short-term and long-term positive outcomes in grafts from donors after brain death (DBD) and after cardiac death (DCD). We report our experience with DHOPE routine application in the treatment over 60 grafts for transplantation.

Methods
We retrospectively analyzed 63 consecutive liver transplants performed after DHOPE with PerLife system, suing a standard Belzer MPS perfusion solution. Temperature was maintained between 4-8°C. Perfusion pressure targets were: 25 mmHg for artery and 5 mmHg for portal vein. Oxygenation was guaranteed supplying 1 L/min pure oxygen to the perfusate. Perfusion parameters (arterial/portal flows, vascular resistances), metabolic markers (lactates trend), and hemodynamic stability were monitored. Perfusate samples were collected at treatment start (t0), 30 minutes after t0 and, afterwards, hourly until the end (tend). Procedure and Post transplant outcomes were recorded.

Results
Between April 2022 and April 2025, 63 grafts underwent DHOPE. The primary indication for treatment was marginal DCD donation. An increasing trend in vascular flows was observed. At the beginning of some treatments, arterial reconstruction was performed while portal vein was perfused. Overall, no device associated graft problems were recorded.

Conclusions
This single-center experience, with routinely performed DHOPE treatments, furtherly confirms the currently available evidences of the safety and the efficacy of this kind of treatment application in liver transplantation.

Introduction
Normothermic-Machine-Perfusion (NMP) could serve as a platform for treatment of marginal livers. Ex-situ administration of mesenchymal-stem-cells (MSCs) exerted multiple positive effects, but the current strategy to apply cell-based therapies during NMP shows some limitations which can affect their effectiveness. To fully harness MSCs benefits, we developed a perfusion system for liver NMP equipped with a MSCs-bioreactor (MSCs-b). The aim of the study was the feasibility of the integration of a MSCs-bioreactor in NMP.

Methods
Different models of Polysulfone hollow- fibers were considered for the application with the purpose of having a material allowing MSC licensing factors in the perfusate to activate the MSC in the bioreactor to produce anti-inflammatory molecules which will then be released in the perfusate and reach the liver by means of perfusate recirculation. The assessment was based on: material inner diameter, active surface, fiber porosity, fiber layout in the housing, minimum/maximum flows allowed. MSCs-b was integrated in the NMP system in a close parallel circuit. (Fig 1).

Inflammatory Mediators Adsorption And Liver Machine Perfusion Strategies

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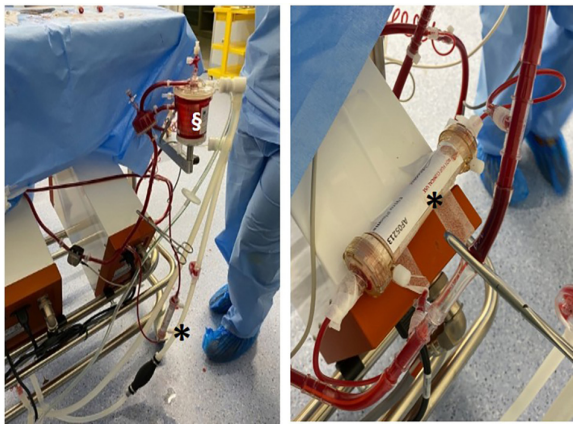

Figure 1 | Connection to the MSCs-b to the liver perfusion device

Table 1 | Bioreactor possible layouts

Characteristics	UM	"Type-1"	"Type-2"
Surface	m^2	0,05	0,075
Inner diameter	µ	300	250
Wall Thickness	µ	85	50
Priming volume (Inner Fibers)	ml	3,9	5
TMP Max	mmHg	100	600
Max Flow	ml/min	20	100
CUT OFF (est)	Da	1,5 Mio	50k

Results

Two types (TYPE 1, TYPE 2) of MSCs-b were deemed suitable. The main characteristics of both types are shown in Table 1. Considering the need of both MSCs cultures on the external side of the fibers and inflammatory mediators and Extracellular vesicle migration to the perfusate towards the organ, the TYPE-1 was selected as the most suitable. The selected MSCs-b was tested both in an *in vitro* feasibility study using rat and pig liver NMP. Filter pressure drop stayed low and transmembrane pressure remained stable through perfusion suggesting no clotting issues. MSCs recovered from bioreactor at the end of perfusion displayed similar vitality and morphology compared with the original cells.

Conclusions

MSCs integration in NMP is feasible and apparently safe for organ perfusion. MSCs seems to express immunomodulatory proprieties.

Introduciton

Machine Perfusion (MP) protects the organs limiting the deleterious effects of ischemia-reperfusion injury (IRI) helping good transplant outcomes. Besides acting as a preservation technique, MP is used also for the implementation of therapeutical treatments targeting some IRI mechanisms. One of these therapeutic approaches is inflammatory mediators adsorption (MA) by apheresis application in MP. We assessed the safety and the efficacy of MA (PerSorb®) combined with both dual hypothermic oxygenated perfusion (D-HOPE) and normothermic perfusion (NMP) with PerLife ® system (Aferetica, Bologna, Italy).

Methods

We selected 12 grafts, already suitable for transplantation, randomizing them to: D-HOPE+MA vs D-HOPE+Non-MA vs NMP+MA vs NMP+Non-MA (**Figure 1**). All D-HOPE and NMP procedures were performed according to routine MP protocols. We compared the four groups assessing perfusate cytokines (IL-1, IL-6, IL-10 and TNF-α) levels at different MP timepoints and post-transplant clinical outcomes outcomes

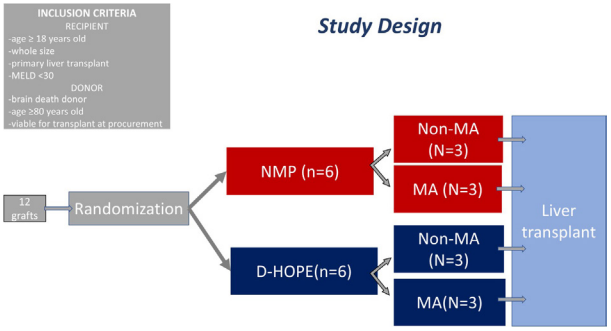

Figure 1 | MP and Adsorption - Study Design

(Intensive Care Unit (ICU) stay, hospital stay, biliary complications and comprehensive complication index (CCI)).

Results

MP procedures were unaffected by MA integration. In D-HOPE procedures, regardless of the use of MA, grafts expressed low cytokines' levels (CKl) than NMP. In NMP, CKL were 10-40 times higher than in healthy subject serum and 20-50 times the D-HOPE ones. Cytokines were removed both in DHOPE and NMP. The concentration-dependent PerSorb® mechanisms of action lead to more remarkable removal in NMP. 2 hours after the beginning of MP, NMP+MA grafts expressed significantly ($p<0.05$) higher arterial flows compared to other groups. No major differences were found in post-operative outcomes, probably due to the small sample size.

Conclusion

Perfusate purification through adsorption of inflammatory mediators in MP is safe, feasible and effective.

The prevention/limitation of inflammatory cascade may improve graft performance during MP and post-transplant outcome. Further studies are needed to explore short- and long-term clinical impacts of this therapeutic strategy.

A136

Inflammatory Changes In Ex-Situ Machine Perfusion With Cytokines Adsorption

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Introduction

The introduction of ex-situ machine perfusion (MP) helped the reduction of grafts discard rate and the testing of grafts' function before transplantation. Cytokines are known to be involved in ischemia-reperfusion injury (IRI). We have recently explored the predictive role and the impact of these inflammatory mediators levels during MP on graft viability and post-transplantation complications, showing a positive correlation between cytokines levels (IL-6, IL-10, TNFa), graft failure and post-operative outcomes. Afterwords, we applied a dedicated immunomodulation technology to reduce these cytokines levels by means of inflammatory mediators adosrption (CDA) through apheresis, in order to restore inflammatory response. The aim of the study is the characterization inflammatory and morphological changes in MP.

Methods

We selected 12 grafts, already suitable for transplantation, randomizing them to hypothermic (D-HOPE) and normothermic (NMP) treatments using PerLife system with PerSorb for CDA: D-HOPE+ CDA vs D-HOPE+Non-

CDA vs NMP+CDA vs NMP+NO-CDA. All D-HOPE and NMP procedures were performed according to routine MP protocols. We compared the four groups assessing perfusate cytokines (IL-1, IL-6, IL-10 and TNF-α) levels (CKL) at different MP timepoints and performing biopsies on the back table (t1), during MP (t2) and at the end of intervention (t3).

Results

MP procedures were unaffected by IMA integration. In D-HOPE, regardless of the use of CDA, grafts expressed lower CKL than in NMP. Cytokines were removed both in D-HOPE and NMP. Higher inflammatory status was observed in NMP, with increased expression in NO-CDA groups (Figure 1), with more inflammatory cells active in NO-CDA grafts, especially at t1.

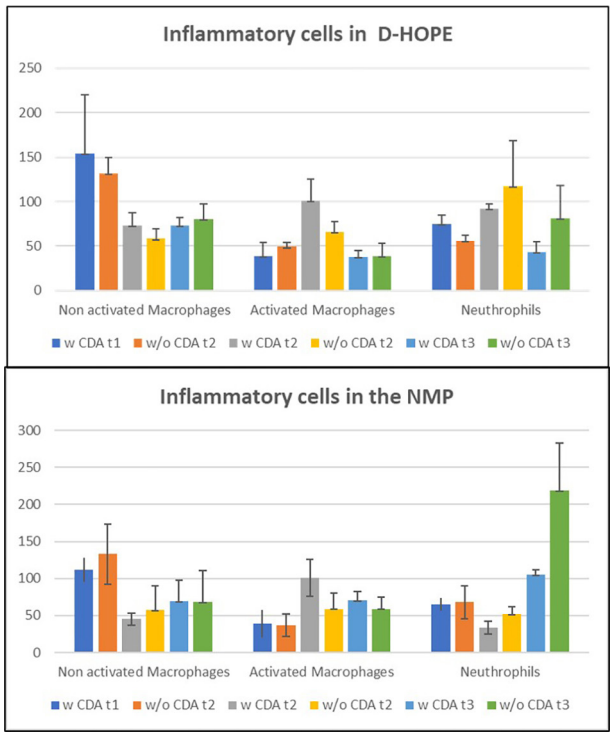

Figure 1 | Inflammatory Cells in D-HOPE and NMP

Conclusion

Perfusate purification through adsorption of inflammatory mediators in MP is safe, feasible and effective.

The prevention/limitation of inflammatory cascade may improve graft performance during MP and inflammatory status. Further studies are needed to explore short- and long-term clinical impacts of this therapeutic strategy.

A137

Controlled Oxygenated Rewarming Without Organ Disconnection: The Efficacy Characterization Of Liquid Exchange In An In Vitro Model

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Introduction

In liver ex-situ treatments, dual oxygenated hypothermia (DHOPE) reduces ischemia–reperfusion injury (IRI) and extends preservation, while normothermia (NMP) enables viability testing. Sequential DHOPE and NMP protocols have been adopted to recover extended criteria donor (ECD) livers. In these protocols, a controlled oxygenated rewarming (COR) allows to move from DHOPE to NMP, avoiding abrupt temperature shifts and additional injury for the organ. Standard DHOPE-COR-NMP protocols require organ disconnection, circuit washout, and re-priming with NMP solution—introducing additional ischemia (~30 minutes) and leaving a residual temperature gap between 12°C and 20°C.

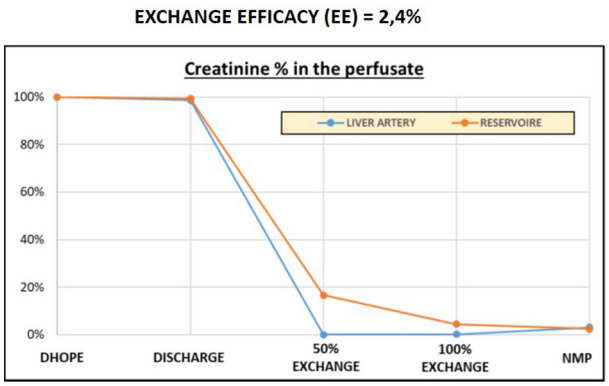

Figure 1 | Exchange Efficacy and creatinine percentual concentration
EE= (Creat5 / Creat0) * 100

Methods

We developed a sequential DHOPE–COR–NMP protocol that avoids organ disconnection. Transition is achieved via a three-step COR (12–35°C): (1) partial discharge of DHOPE perfusate; (2) liquid exchange with Gelofusine; and (3) supplementation with packed red blood cells (RBCs) and additives for the complete NMP perfusate. This protocol was implemented in the PerLife^{PRO} perfusion system. A mathematical model was built to predict residual DHOPE content in NMP. In vitro validation with PerLife^{PRO} employed creatinine as a tracer molecule. Perfusate samples were collected at key points (end of DHOPE, after discharge, after 50% completed and 100% completed exchange, after RBC/additives infusion and normothermia reached). Creatinine concentrations were measured by blinded HPLC. Exchange efficacy was expressed as the percentage reduction from baseline (t_0) to NMP (t_5).

Results

Modeling predicted <0.2% residual DHOPE perfusate after exchange. Experimental testing (n=4 runs, 20 samples) confirmed highly efficient (residual creatinine at t_5 =2.4% t_0) (Figure 1).

Conclusions

This in vitro study shows that DHOPE–COR–NMP without organ disconnection is technically feasible with nearly complete perfusate exchange. The protocol ensures to reach NMP conditions, with no additional ischemia, and minimizes temperature-shift injury, with negligible DHOPE fluid residual.

A138

Perfusion And Adsorption For Liver Grafts Ex-Situ Treatment: A Case Report

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Introduction

The increased use of extended criteria donors (ECD) lead to the growing adoption of ex-situ organ treatments (MP) with many goals: graft injury mitigation, assessment and prolonged preservation prior to transplantation. The aim of this study is to investigate the combination of hypothermic MP (HMP) with inflammatory mediators adsorption by means of the integration of an apheresis device which efficacy was already explored in HMP experimental settings.

Methods

Liver grafts from ECD undergo HMP (temperature <with PerLife system (Aferetica, Bologna, Italy), performing a dual 90 minutes perfusion with the integration of PerSorb (CytoSorbents INC, New Jersey, USA) for inflammatory cytokines remodulation by chemical-physical interaction with the perfusate. Perfusate sampling is performed since the beginning (t_0) until the end (t_{end}), every 30 minutes. In order to assess the efficacy of the removal, pre and post sorbent sampling is performed at each timing. Additional sampling is performed in the static preservation solution, to characterize perfusate cytokine levels before MP start. Target cytokines are IL-6, IL-10, TNF-alfa.

Results
One ECD graft underwent HMP procedure with adsorption inclusion. The average temperature was 8 ± 0,7°C. Target vascular pressures were: 25 mmHg for the artery and 5 mmHg for the portal vein. During the treatment, both vascular resistances decreased (58% arterial, 38% portal) indicating an improval in perfusion conditions. Overall, no complications were recorded. Cytokines have not been analyzed yet.

Conclusion
In this very preliminary experience, cytokine adsorption resulted safe and feasible in high-risk liver treatment. The efficacy of adsorption will be analysed upon cytokine analysis completion.

A139

Controlled Oxygenated Rewarming (COR) In Liver Transplantation – A Case Series

S. Zamboni[1], P. Magistri[1], B. Catellani[1], C. Guidetti[1], R. Odorizzi[1], G. Esposito[1], D. Caracciolo[1], G. Assirati[1], T. Olivieri[1], GP Guerrini[1], S. Di Sandro[1], F. Di Benedetto[1]

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Introduction
Ex-situ liver perfusion (MP) is a strategy used to help the extension of eligibility criteria for liver grafts trying to overcome the problem of the disparity between the suitable organs for transplantation and the number of patients on the waiting list. MP can be performed according to many protocols, mostly differing for the operative temperature and for the goals of the procedure: ischemia-reperfusion injury (IRI) mitigation, prolonged preservation, organ assessment or therapeutical treatment prior to transplantation. We present a case series of grafts treated with sequential protocol (SP), combining dual hypothermic perfusion (DHOPE), slow controlled oxygenated rewarming (COR) of the organ and final normothermic (NMP) treatment in order to perform both IRI limitation and organ viability assessment prior to transplant.

Methods
Liver grafts deemed unsuitable for upfront transplantation were included, considering both extended brain death donors (DBD) or donors after cardiac death (DCD) with macrosteatosis >35%, hemodynamic instability in ICU and during normothermic regional perfusion (NRP) and procurement. All SP protocols were performed with PerLife system, without organ disconnection switching from DHOPE to NMP. Viability was assessed according to Groningen criteria reached within 2.5 h of NMP.

Results
11 liver grafts underwent SP. 2/11 met viability criteria and were transplanted. Transplanted grafts showed a downtrend in lactates. Median time for DHOPE, COR and NRP phases was 120' from 6°C to 12°C, 60' from 12° to 35°C and 225' from 35°C to 37°C, respectively. No procedure or device related complications were recorded. Patients who received grafts deemed suitable had an uneventful postoperative course, with an average hospital stay of 7 days (range 6-8). The median follow-up was 9 months (range 6–12), and both patients are in good general clinical condition with excellent graft function. No biliary complications were observed in either case.

Conclusion
SP is feasible and safe technique for evaluating graft viability prior to transplantation, enabling the use of high-risk donors, expanding the donor pool and increasing the opportunity to transplant more organs without negatively affecting the procedure outcomes.

A140

Liver Defatting Using Rapamycin And Normothermic Ex-situ Perfusion: A Proof Of Concept The RAPAPERF Trial

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Introduction

Steatotic liver grafts, increasingly prevalent due to the global rise in obesity and metabolic syndrome, are associated with poor post-transplant outcomes and are often discarded. Normothermic machine perfusion (NMP) offers a platform for therapeutic intervention, including pharmacological defatting. Rapamycin, a clinically approved mTOR inhibitor, has shown potential to restore lipid homeostasis by downregulating de novo lipogenesis, enhancing autophagy, and—though to a lesser extent—promoting fatty acid β-oxidation through mTOR pathway modulation. This study evaluated a dedicated rapamycin-based formulation for ex-situ defatting of steatotic grafts.

Methods

A pharmaceutical-grade rapamycin formulation was developed for use in ex-situ liver perfusion, with optimized solubility and stability. In vitro studies on steatotic primary human hepatocytes (PHHs) and precision-cut liver slices (PCLS) assessed defatting efficacy and cytotoxicity. The optimized formulation was then tested in a closed-circuit perfusion model without liver, followed by ex-vivo perfusion of porcine and discarded human livers. Pharmacokinetics, metabolic activity, mTOR pathway inhibition and rapamycin's mechanism of action were evaluated.

Results

A stable rapamycin formulation (85% DMSO/15% H_2O, 200 nM) was developed with suitable solubility and 24-month stability. In vitro, rapamycin reduced intracellular triglyceride content by 20–28% in PHHs and PCLS respectively, without affecting viability. In perfused livers, rapamycin reached stable concentrations in blood and bile, with detectable hepatic metabolism. Western blot confirmed inhibition of mTOR signaling via decreased phosphorylation of p70S6K1. In discarded steatotic human livers, rapamycin induced a 22% reduction in triglyceride content without histological evidence of damage. Gene expression analysis by RT-qPCR revealed upregulation of transcripts associated with autophagy (including *LC3* and *SIRT1*) and downregulation of key genes involved in de novo lipogenesis, supporting the proposed mechanism of action.

Conclusion

This study presents the first rapamycin-based formulation specifically designed for ex-situ liver perfusion, demonstrating effective defatting in both preclinical models and human livers. These results support the feasibility of a single-agent defatting strategy using rapamycin and pave the way for early-phase clinical trials.

A141

Clinical Outcomes Of Abdominal Normothermic Regional Perfusion Versus Sequential Hypo- And Normothermic Machine Perfusion: A Single Center Comparison

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Introduction
To address the donor shortage, extended criteria donors after circulatory death (ECD-DCD), are increasingly used. However, ECD-DCD livers bear higher risk of primary non-function and biliary complications. Two main perfusion techniques exist to asses liver function: in-situ abdominal normothermic regional perfusion (aNRP), and ex-situ normothermic machine perfusion, in our center combined with dual hypothermic oxygenated perfusion and controlled oxygenated rewarming (DHOPE-COR-NMP; DCN). This study presents a single center comparison of aNRP and DCN of clinical outcomes of ECD-DCD livers.

Methods
Liver grafts from ECD-DCD donors between October 2018 and the end of December 2023 were included, with a minimum follow-up of 1-year post-transplantation. Livers were categorised as ECD based on factors such as elevated donor laboratory values, or age above 61 years. When the donor was located in the local procurement region and our center was on call for that region, aNRP was performed, otherwise DCN was performed. The primary outcome was death-censored graft survival. Secondary outcomes included acceptance rate, patient survival and post-transplant biliary complications.

Results
In total, 48 aNRP and 37 DCN procedures were performed, which resulted in 36 (75%) and 26 (70%) liver transplantations. At one year, death-censored graft survival and overall patient survival rates were 92% and 97% in aNRP and 94% and 85% for DCN (ns). One-year cumulative incidences of non-anastomotic strictures (NAS), and anastomotic strictures were 8%, and 22% in aNRP and 12%, and 17% in DCN (ns). Bile leaks occurred in 8% of aNRP and 15% of DCN at one year (ns). Complications resulting in a Clavien Dindo score of 3 or higher were observed in 50% of aNRP and 67% of DCN (ns).

Conclusion
The results in this cohort confirm that both aNRP and DCN allow for safe transplantation of ECD-DCD livers with excellent death-censored graft survival and patient survival. There was no difference in the risk of post-transplant biliary complications. In comparison with the NAS occurrence in controls from historical cohorts without machine perfusion, we have shown excellent results.

A142

Sequential Hypo- And Normothermic Perfused Extended Criteria Livers: Two-center Results Of 205 Cases

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Introduction
With the current organ shortage, liver machine perfusion is increasingly used to test and select extended criteria donor (ECD)-livers in an attempt to counter decreasing quality of available organs. Combining sequential oxygenated hypothermic and normothermic machine perfusion, linked by one hour of controlled oxygenated rewarming (DHOPE-COR-NMP) can be used to resuscitate donor livers and subsequently perform viability assessment. We aimed to analyze follow-up data from DHOPE-COR-NMP procedures for ECD-livers performed in two centers.

Methods
All ECD-livers treated with DHOPE-COR-NMP in the Erasmus Medical Center in Rotterdam and the University Medical Center Groningen between March 2019 and October 2024 were included, guaranteeing a minimum follow-up period of 6 months. Livers were classified as ECD based on factors such as elevated laboratory values, or age above 61 years in the case of donation after circulatory death (DCD). The main outcome measure was death-censored graft survival. Secondary outcomes included overall patient- and graft survival, as well as post-transplant complications, such as non-anastomotic biliary strictures (NAS) and anastomotic strictures (AS). Outcome measures were reported at one year and any time post-transplant.

Results
Of the 205 DHOPE-COR-NMP procedures that were performed, 143 resulted in a liver transplant (utilization rate 70%) with a majority of ECD-DCD grafts (n=137, 96%). Death-censored graft survival and patient survival at 1 year were both 92%. Primary non function did not occur in this cohort. Portal vein thrombosis occurred 3 times (2.1%) and hepatic artery thrombosis occurred 5 times (3.5%). The 1-year cumulative incidence of NAS was 5%. Of all NAS cases, 2 patients were successfully re-transplanted and one other case resulted in patient death. At one year, AS occurred in 27% of transplanted livers.

Conclusions
This study illustrates that graft resuscitation and subsequent viability assessment through DHOPE-COR-NMP allows for safe transplantation of ECD-livers with excellent outcomes. The incidence of NAS is low, especially considering the fact that this cohort mainly consisted of high-risk ECD-DCD livers.

A143

End-Ischemic Normothermic Oxygenated Versus Sequential Hypothermic And Normothermic Oxygenated Machine Perfusion For Rescue-Allocated, Major Extended Criteria Donors In Liver Transplantation: A Multicenter, Randomized Controlled Trial – WARM-UP

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Introduction
The widening gap between donor liver supply and increasing transplantation indications has led to broader use of extended criteria donor (ECD) grafts, which carry an increased risk of primary non-function and perioperative complications. Normothermic machine perfusion (NMP) enables functional assessment under near-physiological conditions, improving the safe utilization of ECD livers. However, marginal grafts remain highly susceptible to ischemia-reperfusion injury (IRI). Hypothermic oxygenated perfusion (HOPE) mitigates IRI by restoring mitochondrial function prior to reperfusion. Sequential application of HOPE followed by NMP after controlled oxygenated rewarming (COR-NMP) combines mitochondrial recovery with functional assessment, representing a promising strategy for marginal grafts. While observational clinical data are promising, prospective evaluation against established NMP protocols is still needed.

Methods
WARM-UP is a multicenter, open-label, randomized controlled trial evaluating sequential dual HOPE followed by dual NMP (D-HOPE/D-NMP) versus standard end-ischemic D-NMP in adult recipients of ECD livers allocated via Eurotransplant rescue allocation. Intervention grafts undergo 1–2 hours of D-HOPE, followed by controlled oxygenated rewarming and ≥4 hours of D-NMP. Control grafts receive ≥6 hours of D-NMP alone.

Results
The primary endpoint is a composite of successful graft utilization, no graft loss or patient death at 6 months, and absence of non-anastomotic biliary strictures. Secondary endpoints are discard rate, primary non function (PNF), retransplantation during index stay, Model of Early Allograft Function score (MEAF score), Early Allograft Dysfunction Olthoff criteria, peak AST/ALT until POD7, post-transplant cholangiopathy at six and twelve months, incidence of bile-duct complications, in-hospital mortality and postoperative length of stay, incidence of early rejection within the first three months, incidence of donor-specific antibodies within the first three months, patient survival at six and twelve months as well as graft survival at six and twelve months.

Conclusion
The WARM-UP trial prospectively evaluates whether sequential D-HOPE/D-NMP improves post-transplant outcomes in ECD liver grafts compared to NMP alone. By combining mitochondrial reconditioning and viability assessment, this approach may enhance transplant safety and expand the donor pool. The trial aims to establish an evidence-based end-ischemic perfusion protocol for optimizing ECD liver transplantation.

AA144

In Situ And Ex Situ Extended Normothermic Machine Perfusion In Donation After Cardiac Death In Liver Transplantation

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Introduction
Despite Spain's high organ donation rates, approximately 30% of livers are discarded, and around 10% of patients on the transplant waitlist are lost due to clinical deterioration. Donation after Circulatory Death (DCD) offers a promising solution, yet uncontrolled DCD (uDCD) remains underutilized. Normothermic regional perfusion (NRP) allows in situ organ viability assessment, while ex situ normothermic machine perfusion (NMP) can extend preservation time and improve functional evaluation. Although experience is limited, prolonged ex situ perfusion may enable organ reconditioning prior to transplantation.

Methods
Following ethical approval, we evaluated the feasibility of maintaining viability in livers deemed unsuitable for transplant by extending ex situ NMP beyond 24 hours.

Grafts were perfused using the Perlife® system. The study included grafts from controlled donors and from uncontrolled donors maintained with normothermic regional perfusion (NRP). After procurement, grafts were assessed intraoperatively and transferred for NMP. Perfusion employed a blood-based circuit supplemented with anticoagulants, electrolytes, nutrients, and antibiotics, along with continuous veno-venous hemodialysis (CVVHD) for homeostasis. Liver viability was monitored through biochemical, hemodynamic, and histopathological parameters, assessed at baseline and at 8-hour intervals. Perfusion was stopped upon meeting predefined failure criteria.

Results

The livers were successfully maintained for 58 and 91 hours, respectively. The first case involved a young male cDCD donor with a cold ischemia time of 540 minutes; perfusion was halted due to hemodynamic instability, revealing histopathology showing variable coagulative necrosis, minimal steatosis, and biliary alterations. The second case involved a young male uDCD donor with a 630-minute cold ischemia; perfusion was discontinued due to worsening hemodynamic parameters, with histopathology demonstrating progressive sinusoidal congestion, edema, necrosis, and portal vein congestion over time.

Conclusion

Prolonged ex situ NMP with the Perlife® system is technically feasible and can sustain liver viability beyond 24 hours. This proof-of-concept suggests that previously non-transplantable DCD livers may be reconditioned for transplantation or therapeutic research, potentially increasing donor organ utilization and expanding the donor pool.

A145

Clinical Research With Machine Perfusion Of Swine Livers: Vetlab Experience Of A Pediatric Liver Transplant Center

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Introduction

Liver transplantation is a life-saving therapy for various pediatric diseases. Recent advances in machine perfusion have reduced ischemia time and improved organ preservation and quality [1]. Normothermic machine perfusion (NMP) also enables ex-vivo study of pediatric livers with metabolic disorders, providing a platform to explore alternative therapies [2]. For NMP's research potential, extending perfusion duration is necessary, requiring technological improvements including dialysis and continuous glucose monitoring.

Methods

Six swine livers were retrieved. In the first session (S1), one liver underwent hypothermic machine perfusion (HMP) with a continuous switch to NMP, one underwent NMP with dialysis (VETsmart), one was stored on ice (not perfused), and one was excluded due to damage. In the second session (S2), one liver underwent NMP with dialysis and continuous glucose monitoring, and one served as backup NMP (not analysed). Perfusate samples were collected at predefined intervals. Organ viability was assessed by blood gas analysis, while pressure and flow were continuously monitored. All perfusions used Aferetica's PerLiver system.

Results

In S1, the liver undergoing HMP-to-NMP transition was perfused for 255 minutes, reaching normothermia at 210 minutes without interrupting perfusion. Portal and arterial flows progressively increased during rewarming, although target values were not fully met (Fig.A1). The liver with NMP and dialysis was perfused for 360 minutes, achieving arterial pressure and flow targets. Glucose consumption (Δ110 mg/dL), stable transaminases, and complete ammonium clearance were observed, with dialysis maintaining electrolyte balance (Fig.A2). In S2, the NMP liver was perfused for 30 hours, maintaining stable flows and organ viability up to 600 minutes, with stable electrolytes under dialysis support. The Citsens MeMo glucometer successfully provided reliable real-time glucose monitoring (Fig.A3).

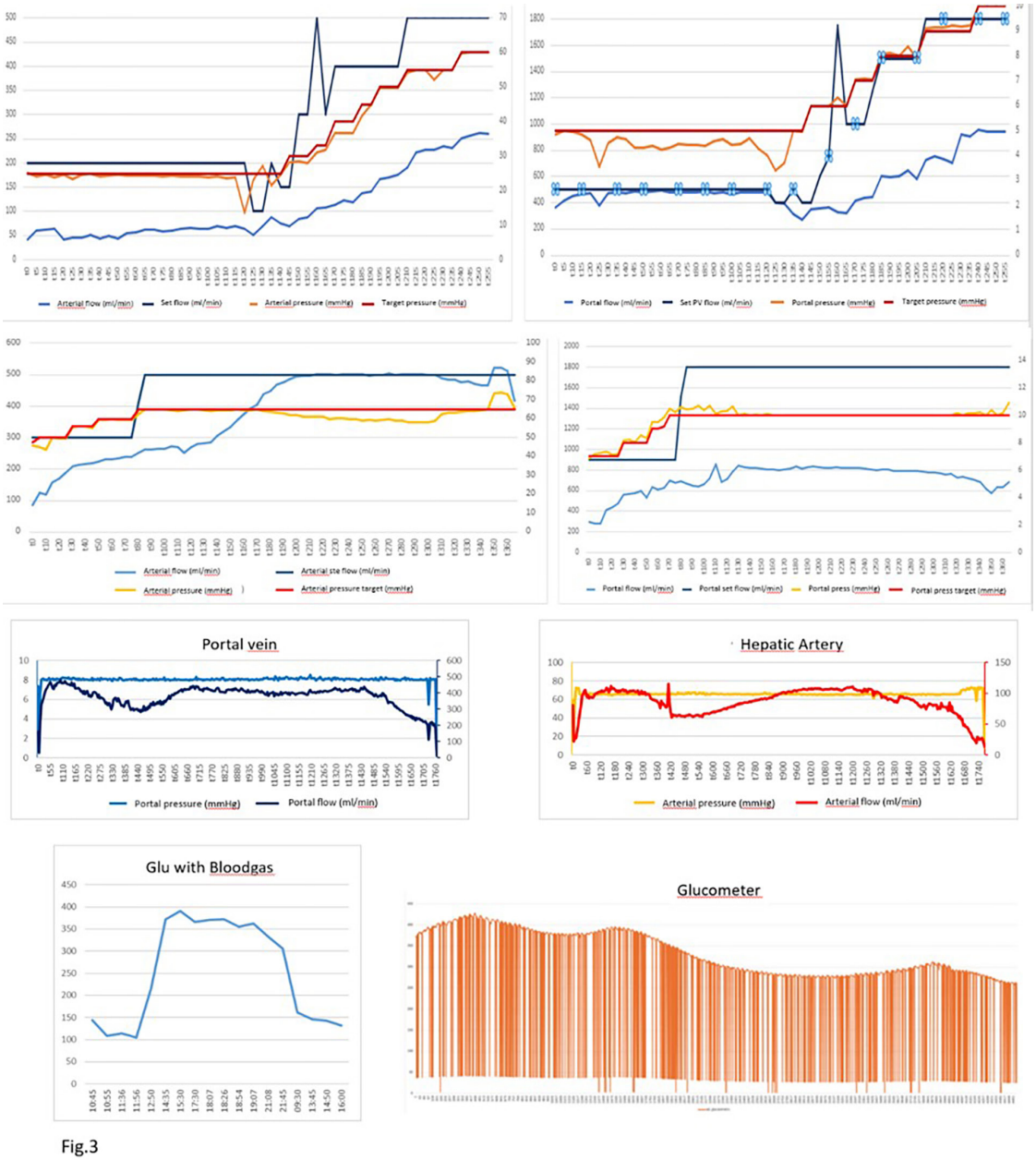

Figure 1 | Portal and Arterial Flows; 2 – Electrolyte Balance; 3 – Glucose Monitoring

Conclusions

The VetLab experience enabled integration of dialysis and glucose monitoring with improved flow management during NMP. However, further studies are needed to develop a fully functional long-term para-physiological ex-vivo perfusion system.

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Kidney Transplantation

A146

Kidney Transplantation From Donors After Cardiac Death With 20 Minutes Of No-Touch Period: Single-Center Experience

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Introduction

The use of kidneys from deceased donors after cardiac death (DCD) is now considered a well-established strategy to address shortage of organs. In Italy law requires 20 minutes of no-touch period that prolongs drastically the warm ischemia period, which can affect organ quality. We present our experience with kidney transplants from DCD donors using normothermic regional perfusion (NRP) *in situ* followed by End-Ischemic Hypothermic Machine Perfusion (EIHP). This combination offers several benefits, mainly reduction in ischemia-reperfusion injury.

Methods

From March 2019 to May 2025, 56 transplants from DCD were performed, including 20 dual kidney transplants (35.7%). The average age of donors and recipients was 60(21-81) and 55(21-73) yo, respectively. Single and double allocation was performed according to our regional guidelines based on age, renal function, and biopsy score data. Donors underwent NRP during procurement, and kidneys were placed in a hypothermic machine perfusion system after bench surgery using two different EIHP systems, Waves IGL®(22 cases) and PerLife Aferetica®(34 cases).

Results

Delayed graft function (DGF) was recorded in 35.7% of cases. In 10% of patients, there was functional DGF (fDGF), while no primary non-function (PNF) was recorded. The mean creatinine at discharge was 2.9 mg/dL (0.9-9.8) and 1.5 mg/dL (0.9-2.9) at 30 days. The average length of stay was 14 days (9-30). The kidneys were perfused in the hypothermic machine for an average of 432 minutes (160-930). The mean arterial flow of the machine perfusion was 98.5 ml/min (60-171); the arterial resistances were 0.219 mmHg per min/ml. The perfusion pressure was 22.8 mmHg (16-28) and the mean temperature was 6.4 °C (4.8 –7.7).

Conclusions

The donation program from DCD donors supported by NRP at procurement and the use of EIHP pre-transplant appears effective and safe. In the absence of PNF, graft survival at 30 days was 100%, achieving optimal organ function. The clinical evaluation of the donor, combined with the physiological response parameters of the organ during normothermic in situ and hypothermic ex vivo perfusion, along with the biopsy score, allows for the implementation of available organs for transplant using this category of donors with reasonable safety.

A147

Single-Center Experience Utilizing Perlife® Oxygenated Hypothermic Perfusion Device In Kidney Transplantation: Outcomes And Predictive Parameters

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Introduction
Between April 2023 and April 2025, 20 renal transplantations were performed at Treviso Hospital using the Perlife® (Aferetica, Bologna, Italy) oxygenated hypothermic perfusion machine for organ perfusion. This study aimed to assess clinical outcomes and identify predictive parameters for renal function.

Methods
Of the 20 transplants, 17 used DCD organs and 3 used DBD. Renal function was recorded at 30 days post-transplant via eGFR. Variables evaluated included "Machine Perfusion Time" (minutes), "Delta Resistances" (initial-final resistance index difference, mmHg/ml/min), and "Final Flow" (flow at perfusion end, ml/min). Multiple linear regression assessed variable influence on one-month renal function, while ROC curves estimated cut-off values for significant variables.

Results
Organs were perfused for an average of 339 minutes. Mean final resistance index was 0.18 mmHg/ml/min (delta 0.1 mmHg/ml/min), and mean final flow was 110.1 ml/min. Average eGFR at 30 days post-transplant was 53.45 ml/min/1.73m^2. (Tab1)

Linear regression showed both "Delta Resistances" and "Final Flow" correlated with post-transplant function. (Tab 2)

A decision tree for "Final Flow" identified a 104 ml/min cut-off: 77% of kidneys below this flow had eGFR < 50 ml/min/1.73 m^2, while 71% above had eGFR > 50 ml/min/1.73 m^2. The 103 ml/min cut-off had an AUC of 0.729, with 0.83 specificity and 0.625 sensitivity. (Fig1-2)

Table 1 | Descriptive Statistics

	Perfusion Time	Initial Resistance	Final Resistance	Delta Resistances	Final Flow	eGFR a 1 month
Mean	339,6	0,287275	0,185175	0,1021	110,1	53,45
Standard Deviation	292,1406294	0,170582861	0,066952708	0,118040537	37,7316006	26,19657471
minimum	77	0,136	0,104	0,015	63	17
maximum	1250	0,775	0,341	0,434	194	98
median	240,5	0,2325	0,1735	0,0585	100,5	46

Table 2 | Linear Regression

Variabile	Coefficiente	Errore_Standard	t_value	p_value
Delta Resistenze	508,62	149,29	3,41	0,01
Flusso al termine	1,29	0,28	4,58	0,00

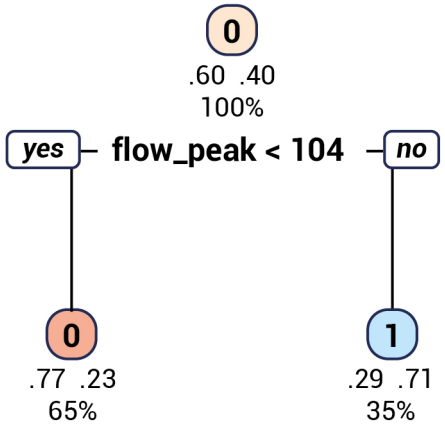

Figure 1 | Decision Tree for "Final Flow"

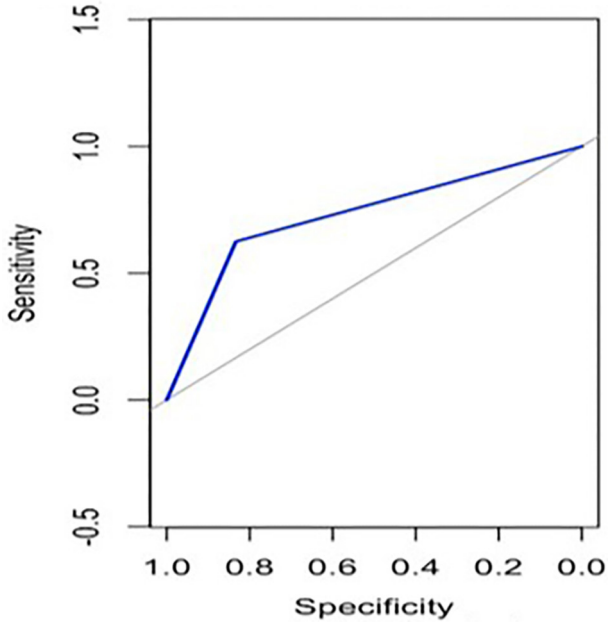

Figure 2 | ROC Curve Final Flow

Conclusions

Renal transplantation with PerLife is safe. "Delta Resistances" and "Final Flow" at perfusion end may serve as indicators for post-transplant outcomes.

Effect Of Hypothermic Machine Perfusion (HMP) On Kidneys Of Expanded Criteria Donors After Brain Death (EC-DBD): A 1-Year Follow-Up Study

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Introduction

Growing availability of kidneys from EC-DBD, which carry a higher risk of worse clinical outcome, has rised the need for advanced techniques, such as HMP integrating classic "Static Cold Storage", to improve the preservation of these organs. The aim of this work was to evaluate the clinical impact of HMP on kidneys from EC-DBD.

Methods

Kidneys from 19 EC-DBD were treated using HMP with the PerKidney system (PerLife, Aferetica), with Pump Protect solution for 6.2 ± 1.5 hours. Recipients underwent a follow-up of 1 year.

Results

13 dual kidney transplantations (DKT) and 5 single transplants were performed, utilized as follows: a) kidneys from 8 donors transplanted according to Karpinski score (KS); b) kidneys from 2 donors declared unsuitable based on KS (7-6; 5-7); c) from 5 donors, despite KS: 6-6, 4-8, 6-4, 6-5, 6-6, DKTs were performed after HMP; d) of 3 donors (despite KS 5-4; 6-4; 4-8) one kidney from each donor was transplanted after HMP, the other one was discarded due to KS and macroscopic evaluation.

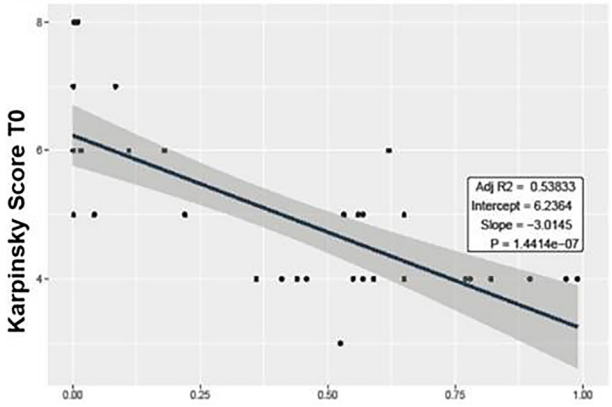

Figure 1A | Resistance Change from Baseline

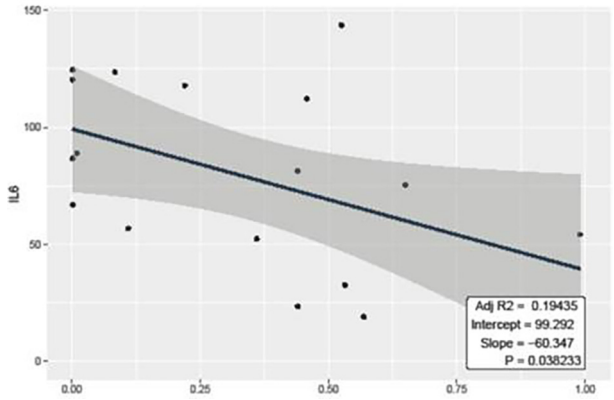

Figure 1B | Resistance Change from Baseline

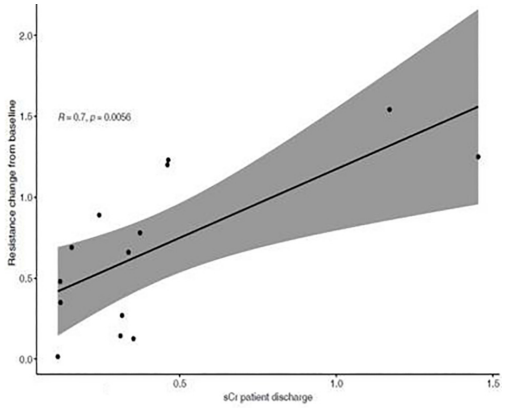

Figure 1C | Resistance Change vs Serum Creatinine at Discharge

Intrarenal resistances (IR) significantly decreased (T0: 1.25 ±0.48, TEND: 0.14 ± 0.270 mmHg/ml/min) during the treatment, with an increase in renal flow. IR drop was inversely proportional to the initial organ score (r2=0.53, p<0.001) [Fig. 1A]. Perfusate analysis revealed a link between resistance changes and IL-6 levels (p=0.03) [Fig. 1B]. Decrease of creatinine correlated with the decrease of resistances (median creatinine after 1-year follow-up: 1.6 mg/dL) [Fig. 1C].

Conclusion

Our experience demonstrated the role of HMP as a support in both the assessment and improvement of organ quality, as showed after 1-year follow-up. Notably, kidneys of 8 donors were successfully used despite clinical, macroscopic, and histological features.

A149

Ischemia-Reperfusion Injury Modulationin Hypothermic (HMP) And Normothermic (NMP) Kidney Perfusion Through pAKT/eNOS Activation

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POWER: A Single-Center, Pilot, Prospective, Randomized Clinical Study Of Hypothermic Oxygenated Perfusion With Or Without Adsorption Of Histologically Evaluated Kidneys Retrieved From Older/Marginal Donors

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Introduction
Hypothermic perfusion of older/marginal kidneys reduces oxidative stress and renal parenchymal resistances, a treatment effect taken as a potential predictor of improved post-transplant function recovery of kidney grafts from marginal donors. We aimed to test whether removal of proinflammatory cytokines, prostaglandins, complement components and other mediators of reperfusion injury by hemo-adsorption during hypothermic perfusion might improve renal vascular resistances in histologically evaluated kidneys from older/marginal donors.

Introduction
The growing use of expanded criteria donors (ECD) grafts for transplantation in order to face the problem of organ shortage leads to the growing need for organ efficient reconditioning strategies also during machine perfusion (MP). Machine perfusion treatments provide the opportunity to improve graft preservation and allow pre-transplant ex-vivo organ treatment. CER-001 has shown clinical anti-inflammatory benefits and renal-protective effects. This study aims at evaluating CER-001 in machine perfusion for IRI modulation.

Methods
In an experimental model of donation after cardiac death (DCD), 20 procured kidneys with 60 min warm ischemia time underwent static cold storage (SCS) for 12h. Oxygenated HMP and NMP were performed for 4 h using PerLife. SCS kidneys were compared with perfused kidneys (PK), dividing PK in CONTROL and CER-001 groups (with 0.4 mg/ml CER-001). Endothelial cells exposed to H2O2, C5a and CER-001 (50-100 µg/mL) were assessed using molecular assays.

Results
During HMP and NMP, CER-001 group expressed significant amelioration of vascular resistances, flows and cytokines levels (CER-001 vs CONTROL, $p<0.05$). CER-001 promoted the activation of SR-BI-pAkt-eNOS pathway leading to the release of protective nitric oxide through eNOS Serine 1177 phosphorylation. In vitro, CER-001 prevents apoptosis and endothelial dysfunction.

Conclusion
The use of CER-001 in MP counteracted vasoconstriction and inflammation, improving renal resistance during the treatment.

Normothermic Machine Perfusion (NMP) And Inflammatory Modulation For Extended Criteria Donor (ECD) Kidney Recovery For Transplantation

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Introduction
Kidney transplantation faces challenges due to the shortage of donor organs, leading to the increased use of ECD organs. Recent advancements in ex-situ organ perfusion technologies have facilitated the use of ECD kidneys by preserving organs in near-physiological conditions to tackle ischemia-reperfusion injury (IRI), a process that triggers inflammatory responses. This study focuses on the application of an inflammatory mediators' modulation (IMM) integrated in a NMP for the recovery of an ECD kidney graft before transplantation.

Methods
This pilot, randomized, single-centre study evaluated the adsorption of mediators of oxidative stress (glutathione S-transferase [GST], lactate dehydrogenase [LDH], and free lactate), acute kidney injury (neutrophil gelatinase-associated lipocalin [NGAL], kidney injury molecule-1 [KIM-1], endothelin, and pro-adrenomedullin), inflammatory cytokines (interleukin-6 [IL-6], interleukin-10 [IL-10], and tumor necrosis factor-alpha [TNF-α]), along with amelioration of renal vascular resistance in five kidney transplants from marginal donors perfused with the Integrated PerLife® system combined with the PerSorb ECOS-300CY™ sorbent (adsorption test group) compared to five marginal kidney transplants perfused without adsorption (non-adsorption control group). Primary outcome was amelioration of renal vascular resistances in the adsorption compared to non-adsorption study group along with safety evaluation of the adsorption procedure. The relationship between pre-implantation histological score and treatment effect on renal vascular resistances will also be evaluated. The study should be completed in approximately 24 months.

Results
From October 2024 to June 2025, three couples of kidneys from three marginal donors were included in the study and perfused: one in the adsorption group and two in the control group. One additional couple of kidneys was randomized but not perfused for technical reasons (drop-out).

Conclusion
Adsorption with the PerSorb® cartridge during hypothermic perfusion should safely ameliorate renal vascular resistances of marginal kidneys, a treatment effect that could reflect amelioration/prevention of kidney reperfusion injury and eventually predict improved post-transplant renal function recovery.

Cytokines' Profiling And Modulation During Normothermic Machine Perfusion (NMP) Of An Extended Criteria Donor (ECD) Kidney For Transplantation

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Introduction

The complex inflammation processes that can take place in the organs during the donation and transplantation steps can lead to both accumulation of the inflammatory mediators in the organ and the endogenous release of those molecules by the organ during the ex-situ treatments resulting in poor transplant outcomes. These mechanisms can be furtherly amplified during machine perfusion, due to the auto-alimentation inflammatory loop taking place with the recirculation of the perfusate and the production/release of the inflammatory mediators by the organ: these inflammatory mediators, such as cytokines, complement and coagulation factors, can be the trigger and the alimentation of important inflammatory responses, leading to an overwhelming inflammation

Methods

Right kidney from an ECD donor (75-year-old female; celebrovascular accident; haemodynamic instability; extreme hypotension) was recovered for transplantation. The discrepancy between right kidney and left kidney Karpinski score (3 vs 7 respectively), together with irregularity of the cortical surface, the presence of severe aortic atherosclerosis without a renal cortex color uniformity after perfusion of preservation liquid, with suspicious areas of remnant donor blood such as lividities, and the presence of a double ureter were key factors in the decision to perform NMP for a more comprehensive assessment of the organ's viability.

A NMP treatment was performed using PerLife ® (Aferetica, Bologna, Italy), in the PerKidney operational mode integrating IMM with PerSorb ® (Cytosorbents Inc., Princeton, NJ, USA), using a blood-based perfusate with a target hemoglobin level of 4-7 mg/dl. Perfusion parameters (pressures, flows, resistance, temperature) were continuously monitored. Perfusate samples were collected at the beginning of the procedure and hourly, until the end of the treatment.

Results

After 320 minutes of NMP, the kidney was successfully transplanted in a 74-year-old woman with a history of end-stage renal disease and a history of 617 days on the waitlist. No side effects were observed associated with the use of PerSorb. The post-operative course was uncomplicated with no delayed graft function (DGF), with 1,1 mg/dl serum creatinine level at 6 months follow up.

Conclusion

NMP treatment with PerLife integrating PerSorb for inflammatory mediators modulation resulted in a safe and feasible treatment of recovery of an ECD kidney for transplantation. Further studies are needed to explore the long-term clinical impact of this approach on graft survival and function.

and, consequently, aggravating ischemia-reperfusion injury (IRI). The purpose of this study is a preliminary characterization of inflammatory mediators and their adsorption by apheresis applied during the NMP treatment in an ECD kidney for transplantation.

Methods

Right kidney from an ECD donor (75-year-old female; celebrovascular accident; haemodynamic instability; extreme hypotension) underwent 320 NMP treatment with PerLife using PerSorb for inflammatory mediators' adsorption. Perfusate samples were collected hourly until the endo of the treatment. To characterize the efficacy of the adsorption pre- and post- PerSorb sampling was performed.

Results

After NMP, the kidney was successfully transplanted in a 74-year-old woman. The cytokines characterization is showed in Figure 1, revealing a marked increase during the treatment. PerSorb actively adsorbed 19.232.600 pg of cytokines, mostly IL-6, IL-8, MCP1, GCSF, RANTES, HGF, TNFa, in a concentration-dependent mode.

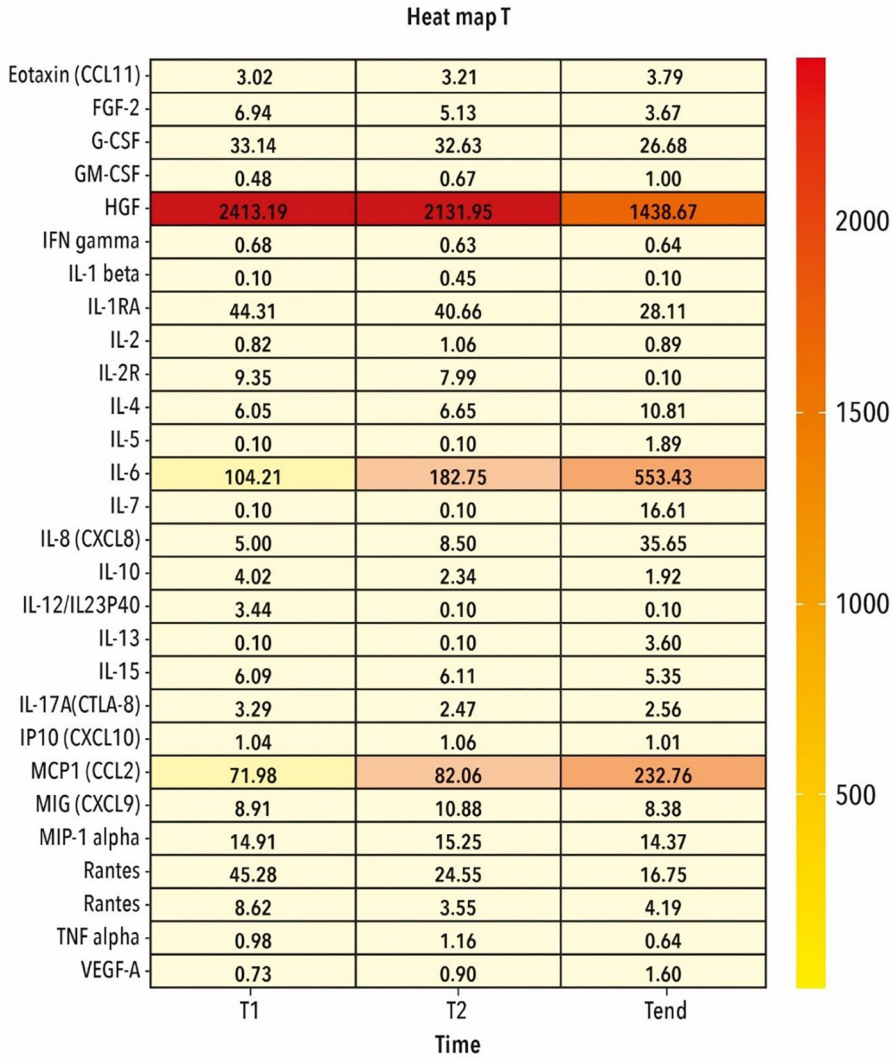

Figure 1 | Cytokines' Profiles (pg/ml) over time during NMP Treatment (T1 – 1h after NMP start; T2 – 1h after T1; Tend – NMP end)

Conclusion
Inflammatory mediators significantly increased during NMP. At the same time, PerSorb® remarkably and efficiently reduced cytokine levels resulting in optimal organ perfusion. Further studies are needed to e deeply explore the clinical impact of this immunomodulation therapy in NMP.

A153

Hypothermic Perfusion With The Adsorptive Cartridge Persorb Limits Ischemia-Reperfusion Injury Of Pig Kidneys By Sustaining Mitochondrial Function And Inhibiting Senescence Of Tubular Epithelial Cells

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Introduction
Hypothermic perfusion limits kidney ischemia-reperfusion injury (IRI) and Delayed Graft Function (DGF) in high-risk donors, prolonging graft survival. Study aim: to evaluate the protective effect of the sorbent cartridge PerSorb on mitochondrial dysfunction and senescence of pig kidneys during hypothermic perfusion.

Methods
Pig kidneys were subjected to hypothermic perfusion with (n=6) or without (n=6) Persorb (Aferetica srl, Bologna, Italy) for 4 hrs. Histology, gene expression of KIM-1, NGAL, TNF-α, IL-6 or Klotho, levels of citric acid cycle enzymes, ATP and mitoROS production were evaluated in kidney samples. Metabolomics analysis of tryptophan pathways by LC-MS/MS and quantification of extracellular vesicles (EVs) by Nanotrack analysis (NTA) were also performed n liquid perfusion samples. All data were compared with non-perfused kidney pair (n=6).

Results
In comparison to cold storage, hypothermic perfusion with PerSorb reduced tubular injury score, NGAL, IL-6 and Klotho gene expression. PerSorb also increased citrate synthase, malate dehydrogenase and succinate dehydrogenase levels, ATP production and mitochondrial electron transport chain, concomitantly reducing mitoROS. Metabolomic analysis of tryptophan metabolism showed the presence of a limited number of solutes including tryptophan (Trp), nicotinamide (NAM), nicotinamide mononucleotide (NMN), Nicotinic Acid (NA), nicotinamide riboside (NR) and Indoxyl Sulfate (IS). Of note, PerSorb was able to adsorb the nephrotoxic compound IS and other indole derivates such as indole-3-pyruvic acid (I3PA), indole-3-carboxaldehyde (I3A), 3-indoleacetic acid (I3AA), tryptamine (TRYP), indole-3-propionic acid (IPA), 3-indoxyl sulfate potassium salt (IS), and melatonin (5-MT). Last, PerSorb reduced in the perfusate the concentration of EVs released by damaged and inflamed cells and potentially involved in tissue damage. All the described protective effects were more pronounced in presence vs. absence of PerSorb in the perfusion circuit.

Conclusions
Hypothermic perfusion with the adsorptive cartridge PerSorb can limit kidney IRI by sustaining mitochondrial function and inhibiting senescence of tubular epithelial cells. Further experiments including a higher number of organs and/or human kidneys discarded from the clinical use are needed to confirm these preliminary results.

A154

Incidence And Clinical Relevance Of Acute Kidney Injury (AKI) In Hospitalized Renal Transplant Recipients: Correlation With Delayed Graft Function (DGF) And With Acceleration Of Graft Failure

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Introduction
Kidney transplantation (KTx) is the most effective therapy for end-stage chronic kidney disease. However, complications such as Delayed Graft Function (DGF) and Acute Kidney Injury (AKI) accelerate graft failure by reducing Renal Functional Reserve (RFR). While AKI is a recognized risk factor in hospitalized patients, its incidence and impact in KTx recipients are less defined. This study evaluated the incidence, causes, and prognostic significance of AKI in KTx patients, with focus on its relationship to DGF and survival.

Methods
We conducted a monocentric, retrospective study of KTx patients admitted to our University Hospital between 2019 and 2023. AKI was identified and staged according to KDIGO criteria based on serum creatinine. Incidence and distribution were compared with the overall hospitalized population (n=94,278). DGF was defined as dialysis within the first week post-transplant. Outcomes were assessed with a follow-up of about 25 years.

Results
The KTx cohort included 745 admissions (0.7% of hospitalizations), median age 55 years, 65% male, 85% first transplant. AKI occurred in 199 cases (26.7%): Stage 1, 73.3%; Stage 2, 14.6%; Stage 3, 15.2%. Compared to the general population (AKI 16.7%), transplant patients had higher incidence but more mild cases. Main causes were infections (29.3%), immunologic complications (23.4%), and obstructive/urologic events (17.4%). AKI significantly reduced patient and graft survival regardless of etiology. Notably, 16.1% of AKI cases had prior DGF, which independently increased risk of subsequent AKI (HR 1.6). Patients with both DGF and AKI showed the poorest survival outcomes.

Conclusion
AKI episodes are frequent in KTx recipients and independently compromise long-term patient and graft survival. Prior DGF increases susceptibility to AKI, underscoring the need for preventive strategies during hospitalization and strict follow-up after discharge. Optimized immunosuppressive and nephroprotective management is essential to limit accelerated graft senescence and failure.

A155

Ex Situ Normothermic Kidney Perfusion: Setting Up Of A Long-Term Protocol

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Introduction
Normothermic machine perfusion (NMP) is increasingly used to recondition donor kidneys, particularly marginal organs, prior to transplantation. It provides near-physiological conditions that help limit ischemia-reperfusion injury (IRI) and allows functional assessment. Long-term NMP—extending to days—opens new possibilities for repair and regeneration, though standardized protocols are lacking. This study establishes 3-days NMP protocol using a porcine model and evaluates metabolic performance and perfusate management.

Methods
A porcine model was developed for heart-beating kidney procurement for functional and metabolic ex vivo assessment of perfused kidneys using the PerLife system. As the organs were transported under cold static storage, a rewarming phase was performed to gradually bring the organ from hypothermic to normothermic conditions without sudden perfusion condition changes (temperature, pressures, liquids). To guarantee the proper oxygenation of the organ, an oxygen concentrator was used to infuse 93% oxygen in the oxygenator module. After reaching NMP, arterial and venous electrolytes, lactate, glucose, haematocrit, pH, pO2 and pCO2 were monitored every 30 minutes until stabilization and then every 4 hours. Oxygen consumption, lactate and glucose clearance were used as markers of metabolic status. Urine was recirculated in the perfusate.

Results
Kidneys were metabolic active after reaching normothermia, with oxygen consumption and CO_2 production confirming active respiration. Venous pO_2 of 25 mmHg maintained oxidative phosphorylation and stabilized lactate levels. Early trials showed that CO_2 infusion was necessary for pH buffering and consistent oxygenation, which was validated in a pilot experiment. A glycolytic shift emerged after 12 hours, evidenced by glucose use, lactate production, and increased renal resistance. When CO_2 was added, the shift remained oxidative without lactate buildup. Principal component analysis identified two metabolic profiles: one supporting diverse energy production through fatty acid oxidation and lactate synthesis, and another emphasizing oxidative phosphorylation and lactate clearance.

Conclusion
This extended NMP protocol represents a viable model for long-term ex vivo kidney perfusion. Controlled oxygenation and acid-base balance are achievable through targeted O_2 and CO_2 infusion. The observed glycolytic switch marks a limiting factor in long-term perfusion, and the data suggest that introducing metabolic substrates for fatty acid oxidation could enhance stability and function.

Pancreas Transplantation

A156

Hypothermic Ex-Situ Perfusion And Inflammatory Mediators' Characterization: A Preliminary Experience Of Pancreas

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Introduction
Several experimental settings have explored the role of ex-situ machine perfusion (MP) in pancreas preservation, focusing also on the effects on parenchymal oedema or tissue damage. One of the main goals of MP is to protect the graft from the ischemia-reperfusion injury (IRI), negatively affecting the transplant outcomes. The mechanisms underlying MP protective effects are still to be fully characterized. In this report, we describe a preliminary feasibility study on the application of inflammatory mediators (IM) adsorption to strengthening the IRI mitigation in pancreas MP.

Hypothermic Ex-Situ Perfusion: The Feasibility Study On Pancreas

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Introduction

Increasing use of donors after cardiac death (DCD) lead to a new interest in the organ perfusion as a preservation and evaluation platform. The clinical standard for pancreas preservation for transplantation is static cold storage (SCS). Hypothermic oxygenated ex-situ perfusion (HOPE) has shown advantages over SCS in other abdominal organs preservation. Some animal and human experimental models have already explored the feasibility of these technique in pancreas preservation. In this report we present an application of HOPE, adapted from a certified kidney HOPE configuration, for the evaluation of a pancreas graft procured form a controlled DCD for transplantation.

Methods

After procurement and 8h of SCS, the graft was prepared for perfusion adapting the kidney operational mode and disposable kit (PerKidney) of the PerLife system: Kidney organ container for organ placement, Arterial line for iliac artery perfusion, urine collection bag for duodenal liquid collection. The vein drained freely in the liquid reservoir. Perfusion parameters (pressure (P), flow (F), temperature (T), vascular resistance (VR)) were recorded at the beginning and hourly, until the end of the procedure. Target P, T were established according to recently published recommendations (Consensus Conference Guidelines, TRANSPLANTATION LEARNING JOURNEY, 2022) and set, respectively to 30 mmHg and 5°C. Perfusate and duodenal liquids sampling was performed every 30 minutes for biochemical characterization.

Methods

The pancreas from a 23-years-old donor after cardiac death and 8h of SCS was perfused in hypothermic oxygenated (HOPE) modality with PerLife system, adapting the pressure-controlled PerKidney operational mode with target temperature at 5 °C, target pressure at 30 mmHg. A standard acellular abdominal organs' hypothermic perfusate was used. The perfusion was combined with the application of the PerSorb device within the circuit in order to adsorb IM from the perfusate (flow rate: 300 ml/min) and lower the inflammation burden. To characterize the effects, perfusate sampling was performed before and after PerSorb and within the duodenal secretion bag to dose Il-6, Il-10 and TNF-alfa levels. In order to modulate duodenal resistance, mannitol and albumin were added to the perfusate as impermeant for a proper osmotic pressure. Due to duodenal secretion at 2h 20 minutes 1 L of fresh perfusate was added to reestablish the volume levels.

Results

In 187 minutes of treatment, the total levels of cytokines within the perfusate were below detectable values, while in the duodenal secretion the target cytokines rose. IL6 peaked 1h: 997 pg/ml; IL-10, TNF-alfa peaked at 2h: 174 pg/ml; 239 pg/ml, respectively. The addition of fresh perfusate, mannitol, albumin, determined the lowering of the cytokine's levels at 160 minutes. At 180 minutes, the duodenal cytokines levels were peaking again: 746 pg/ml (IL-6), 59 pg/ml (IL-10), 92 pg/ml (TNF-alfa).

Conclusions

Purification during pancreas HOPE is safe and feasible. Further studies are needed to deeply explore the inflammatory response of the graft and the potential role of IM adsorption for IRI mitigation in this setting.

Results
The graft was perfused for 187 minutes recording the following parameters: T = 5.1±1.2 °C; F= 100±4 ml/min; VR=0,172±0.006 mmHg/ml/min. During HOPE, F progressively increased, resulting in a VR decrease. 1 L of pancreatic and duodenal secretion liquid was collected, requiring additions of perfusate liquid after 1h of procedure. A slight increase of lactates was recorded (1,6 to 2,0 mmol/L). at 1h 47 minutes, to reduce the duodenal tension, 18% Mannitol and 20% Albumin were added to the perfusate, positively influencing organ resistance decrease.

Conclusions
The procedure resulted to be safe and feasible with no device-related complications recorded. Further studies are required to develop a fully dedicated pancreas operational mode for ex-situ treatment for transplantation.

Eye Ex-Situ Perfusion

A158

ECaBox "Eyes In A Care Box" Project: Regenerating Human Retina From Resuscitated Cadaveric Eyes

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Introduction
In the last decade, basic and translational research dramatically expanded the development of new drug and regenerative therapies. Preclinical research still lacks adequate models of human organs and even though human organoids approaches are a major step forward in mimicking physiological conditions, they fail to reflect the overall tissue physiology and complexity. Human dissected retinae and non-vascularised human eye organoids fail to recapitulate the vascular and tissue systems.To address these needs, the ECaBox project aims to develop a dedicated platform, the ECaBox (Eyes in aCare Box) to resuscitate the human cadaveric eye while ensuring eye function and structure ex vivo.

Methods
To develop the EcaBox technology, a multidisciplinary and international consortium was assembled, including experts in biology, biotechnology, modelling, engineering and physics. One of the main objectives was to develop a functioning prototype to assess the regeneration and functional rescue of the eye. The team defined high level requirements in terms of: organ containment, liquid containment and hydration, liquid recirculation and oxygenation.

Results
We developed a prototype that enabled perfusion and resuscitation of ex vivo eyes under defined conditions. Using this system, retinal cellular viability, vascular integrity, and overall eye functionality were maintained for at least three hours post-mortem. While further testing is ongoing, these preliminary outcomes support the feasibility of post-mortem ocular support using our first-of-its-kind ECaBox system.

Conclusion
The ECaBox should have an enormous impact in advancing regenerative medicine by providing an intact human organ to explore and analyse regenerative processes *ex*

situ, allowing to: resuscitate human eyes to test human eye therapies ex situ, serve as a proof of concept to develop therapies also in other organs contributing to reduce the current gap between the organ demand and the suitable organ availability for transplantation.

O_2 In Ex-Situ Perfusion

A159

What Is The Quantity Of Oxygen Added To The Perfusate In Hypothermic Machine Perfusion?

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Introduction
Hypothermic Oxygenated ex-situ organ machine perfusion (HMP) is one of the strategies used to overcome the existing gap between the available organs and the suitable organs for transplantation, helping reducing the number of patients waiting for the intervention. HMP can be implemented operating on temperatures (T) below 12°C and using systems that allow active oxygenation to the perfusate with the direct administration of oxygen to the perfusate or with the transfer of oxygen by an oxygenator connected to the gas supply. The low T corresponds to low metabolic rates and, consequently, lower oxygen demand than in "in-body" conditions. In HMP, the oxygen reaching the organ is dissolved in an acellular, aqueous perfusate. In this report, we characterize the amount of oxygen available in the perfusion solution during HMP, focusing on the standard perfusate solution used: Belzer UW MPS (BUW) solutions.

Methods
We characterized the oxygen solubility ($solO_2$) in BUW focusing on the main influencing factors: salinity of the solution (sBUW) associated with BUW composition, T range 4-12°C, different quantity of oxygen administred, expressed as different partial tentions of oxygen (pO_2) and the atmospheric pressure of 1 atm. We used these factors to determine the amout of oxygen [O_2] (mg/L, ml/L) corresponding to many different conditions, by applying a validated online calculator to iteratively solve the Debye–Hückel theory limiting laws for unideal solutions (DHUS), expressing the existing relationship between the $solO_2$ and all the considered parameters.

Results
After determining sBUW= 34.590 ppm, we calculated the corresponding [O_2] at different HMP T and O_2 administration conditions, confirming that given a pO_2 level, higher T leads to lower O_2 dissolved in the BUW solution.

Conclusions
The amount of O_2 administered to the organ is associated with the perfusate flow towards the organ and [O_2] in the perfusate. As the BUW is carrier-free, the O_2 reaching the organ corresponds to the dissolved O_2 in the perfusate. The relationship among O_2 content in BUW, pO_2 and T follows DHUS and indicates that higher T is associated to lower O_2 at constant pO_2.

A160

What Is The Quantity Of Oxygen Added To The Perfusate In Normothermic Machine Perfusion?

A. Kurevija[1], V.Marassi [2,3], S. Giordani[2,3], A. Placci[2,3], B. Roda[2,3], E. Panetta[1], A. Zattoni [2,3], M. Atti [1], P. Reschiglian[2,3]

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Introduction

Normothermic machine perfusion (NMP) is one of the ex-situ perfusion protocols established for the recovery and the treatment of grafts for transplantation. In the current practice, NMP is performed recirculating a perfusate at 37°C from and towards the organ to be transplanted, providing the proper grafts' metabolic support by oxygen, nutrients and/or drugs administration. As NMP simulates the in-body envirment the metabolic rate of the graft is the near-physiological one. This is the main reason why the NMP perfusate needs to be added with oxygen carriers such as packed red blood cells (RBCs). The aim of this report is to characterize the oxygen content [O_2] (mg/L; ml/L) in NMP perfusate.

Methods

We characterized: the state of art of perfusate compositions reported for NMP perfusions, focusing mainly on liver and kidney protocols; the relationship between [O_2] and the main components of the perfusate, the [02] associations with environment conditions (pO_2, Temperature (T)). We defined the [O_2] resulting in the most commonly used perfusate compositions.

Results

The overall protocols report the use as RBCs as source of oxygen carriers (hemoglobin (Hb)) in NMP. With this type of perfusate, considering the Hb- O_2-binding properties, 98% of O_2 is transported by Hb, while 2% is dissolved in the perfusate. At constant T=37°C, Hb results fully (>98%) saturated at pO2=100-110 mmHg. Each gr of Hb transports 1,36 mlO_2. Considering 2.2 L of NMP perfusate with Hb< 5 g/dL, resulting in total volume <133,2 mlO_2 when Hb is 98% saturated.

Conclusions

The amount of O_2 in NMP perfusate is mainly depending on the quantity of O_2-carrier content in the liquid and on how much this carrier is saturated. Over-physiological pO2 do not significantly contribute to increase O_2 as the Hb is fully saturated at pO_2=100-110 mmHg.

A161

The Role Of Perfluorocarbon-Based Nanodroplets In Machine Perfusion

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Introduction

Perfluorocarbon-based nanodroplets are emerging as promising tools in advanced medical imaging and therapeutic applications, particularly in the fields of tissue engineering, vascular interventions, and drug delivery. Graft perfusion, which refers to the process of ensuring adequate nutrients and oxygen supply to transplanted organs, plays a critical role in the survival and function of grafts. Efficient graft perfusion can be enhanced by utilizing perfluorocarbons (PFCs), which possess unique properties, such as high oxygen-carrying capacity, low viscosity, and biocompatibility. Furthermore, their small size allows for enhanced tissue penetration and improved distribution within the body, making them ideal candidates for monitoring and enhancing graft survival in transplant and regenerative medicine. We report an experimental study of PFCs performed to assess the basic characteristics of these additives and their potential use in machine perfusion (MP).

Methods

We tested perfluorocarbon Nanodroplets coated with dextran and low molecular weight chitosan at room (22°C) and body temperature (36-37°C) in an experimental setting using a simple circulating perfusion apparatus to assess the oxygen levels in a special perfusate.

Results

The tests were conducted on special medias, like dulbecco and gelofusine solutions in order to simulate

the real-life perfusates of normothermic machine perfusions, checking if PFCs can be a valid alternative to packed red blood cells, to provide stable and efficient mass of oxygen during the treatment. Dissolved oxygen was measured and 20 mg/L was the oxygen concentration in short-time perfusion (1-2 h).

Conclusion

PFC may constitute a promising alternative to red blood cells during MP. Further experiments are needed to fully characterize these additives potentials and benefits in MP.

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