Hemoadsorption in burns

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Conflicts of Interest

Scientific partnership with the following companies:

- Vantive
- BBraun
- Biomérieux
- Estor/Toray
- Exthera
- Fresenius Medical Care
- Infomed
- Jafron
- Cytosorbents
- Norrdia

Outline

1) Severe burns: the classic clinical story

2) Hemoadsorption in burn patients: what is the evidence?

Outline

1) <u>Severe burns: the classic clinical story</u>

2) Hemoadsorption in burn patients: what is the evidence?

Patient from the Lyon burn center

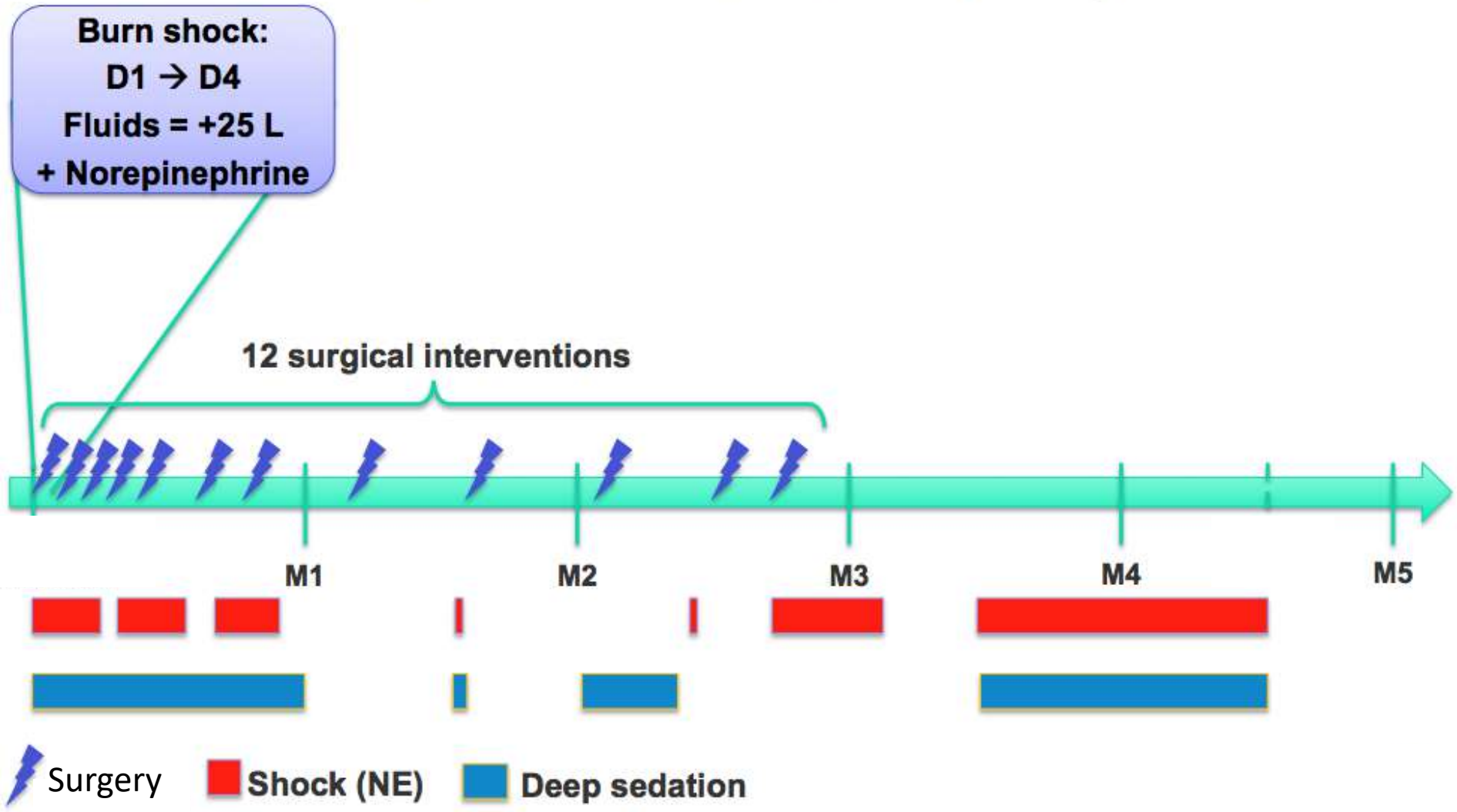
- Man, 68 years old, 1 m 71 – 84 kg

- Past medical history:
  - High blood pressure
  - Mild Chronic Kidney Disease (stable)

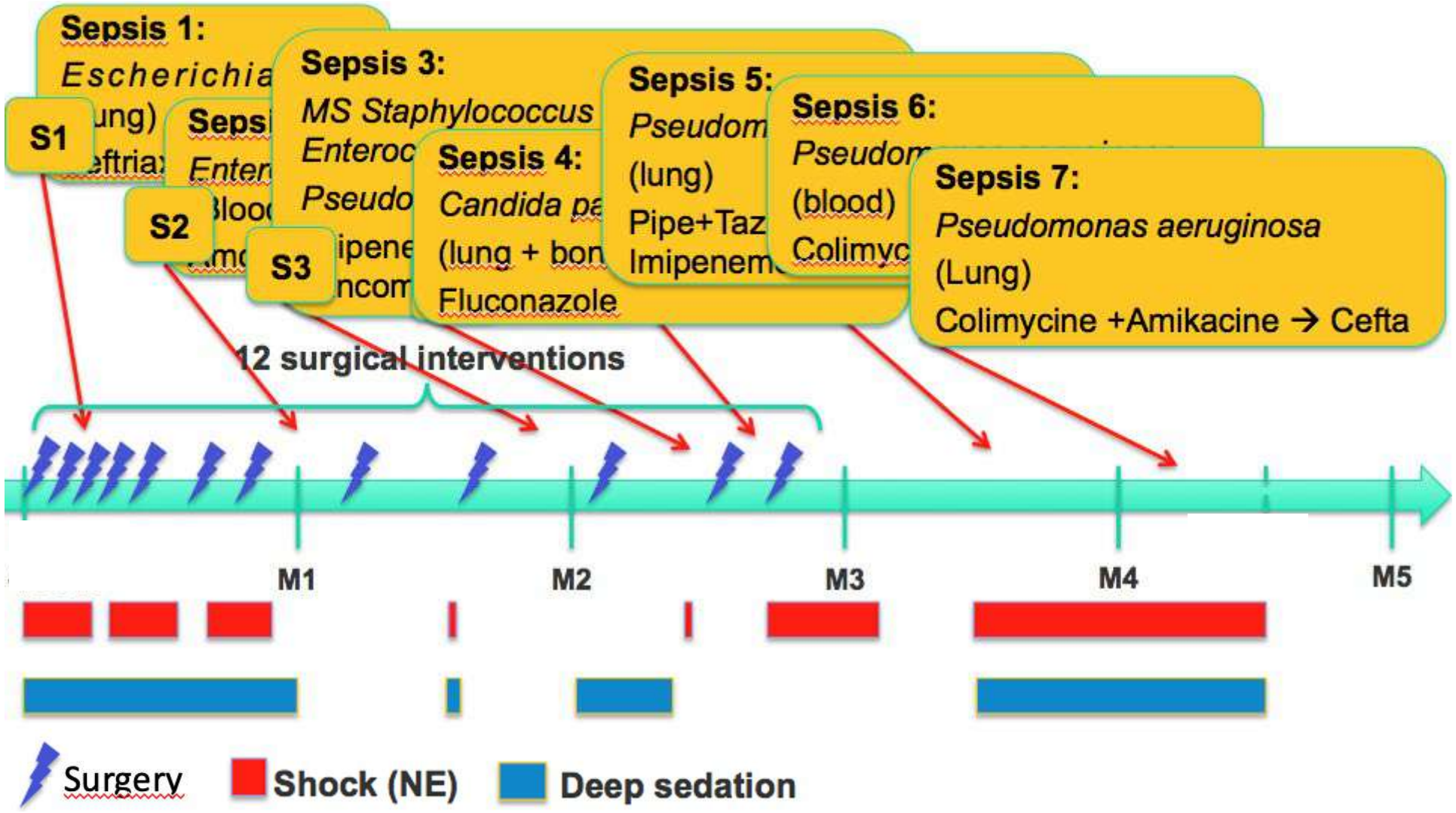
- Admitted to our burn ICU due to:

- **<u>Domestic accident – Fire at home</u>**
  - Total burn surface area (TBSA) = 50% (3rd degree = 45%)
  - Face, back, thorax, upper limbs and both hands

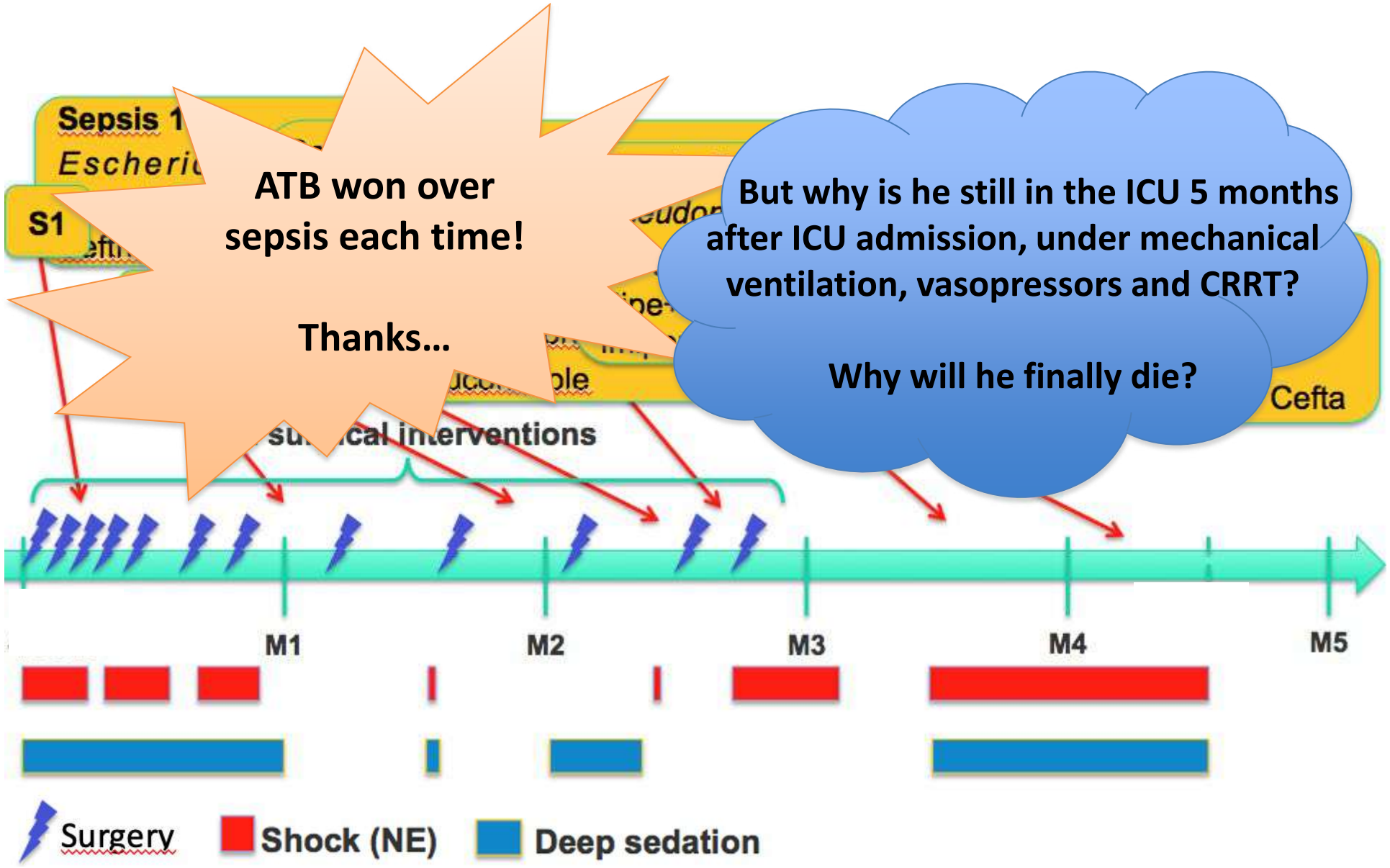
Patient from the Lyon burn center



Patient from the Lyon burn center



Patient from the Lyon burn center



Immunosuppression +++

mHLA-DR : robust maker of immunosuppression

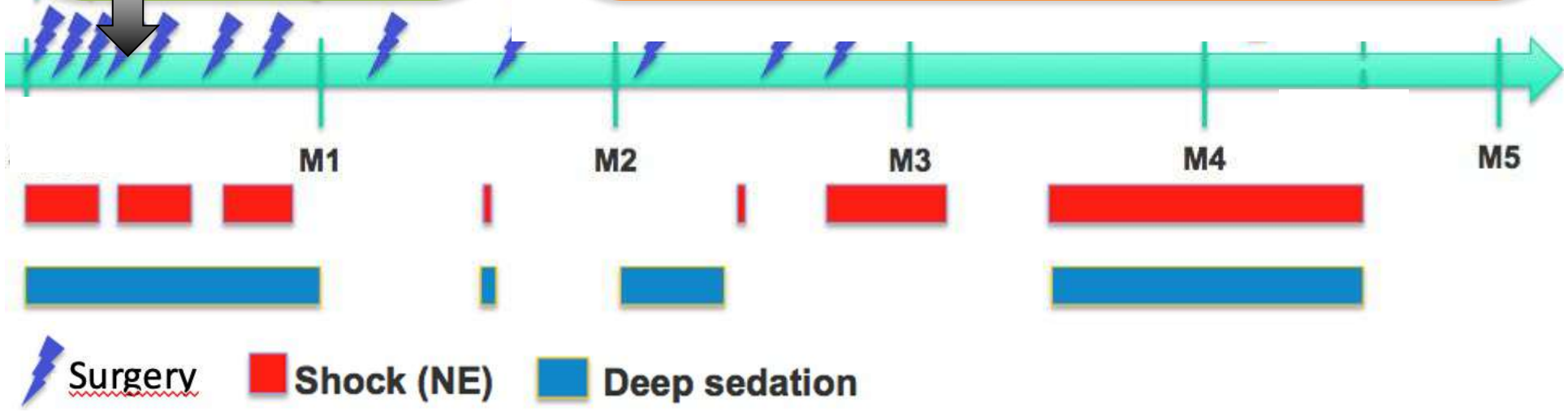
mHLA DR 10 days after admission

=

2568 AB/C

mHLA DR

- > 20 000 AB/C = Normal
- 15 000 to 20 000 AB/C = Grey zone
- 10 000 to 15 000 AB/C = Light immunosuppression
- 5 000 to 10 000 AB/C = Moderate immunosuppression
- < 5 000 AB/C = Severe immunosuppression



Immunosuppression +++

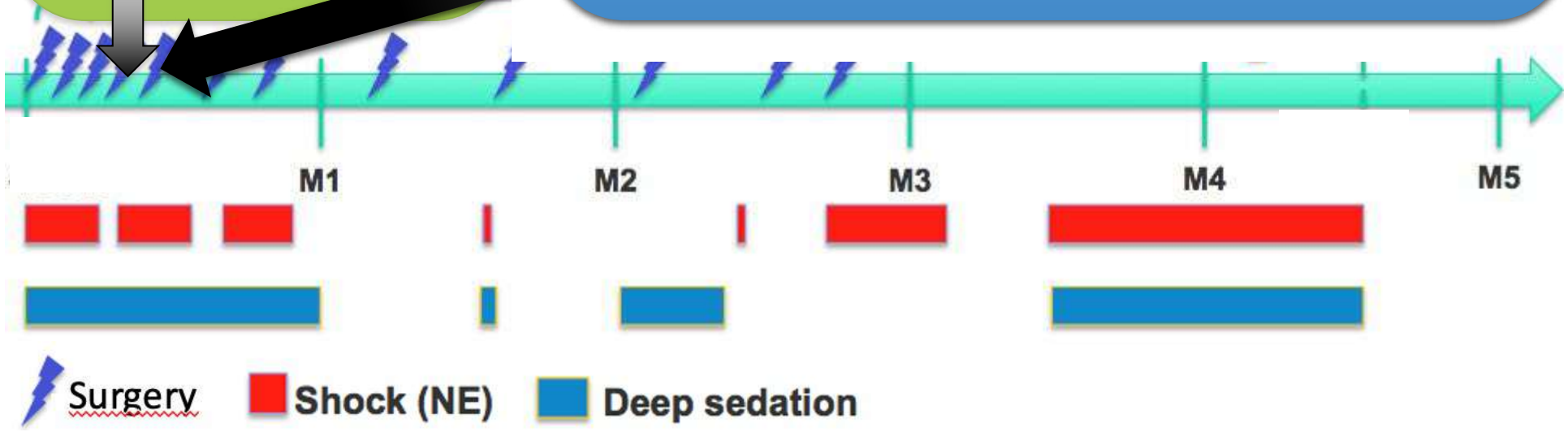
mHLA DR 10 days after admission

=

2568 AB/C

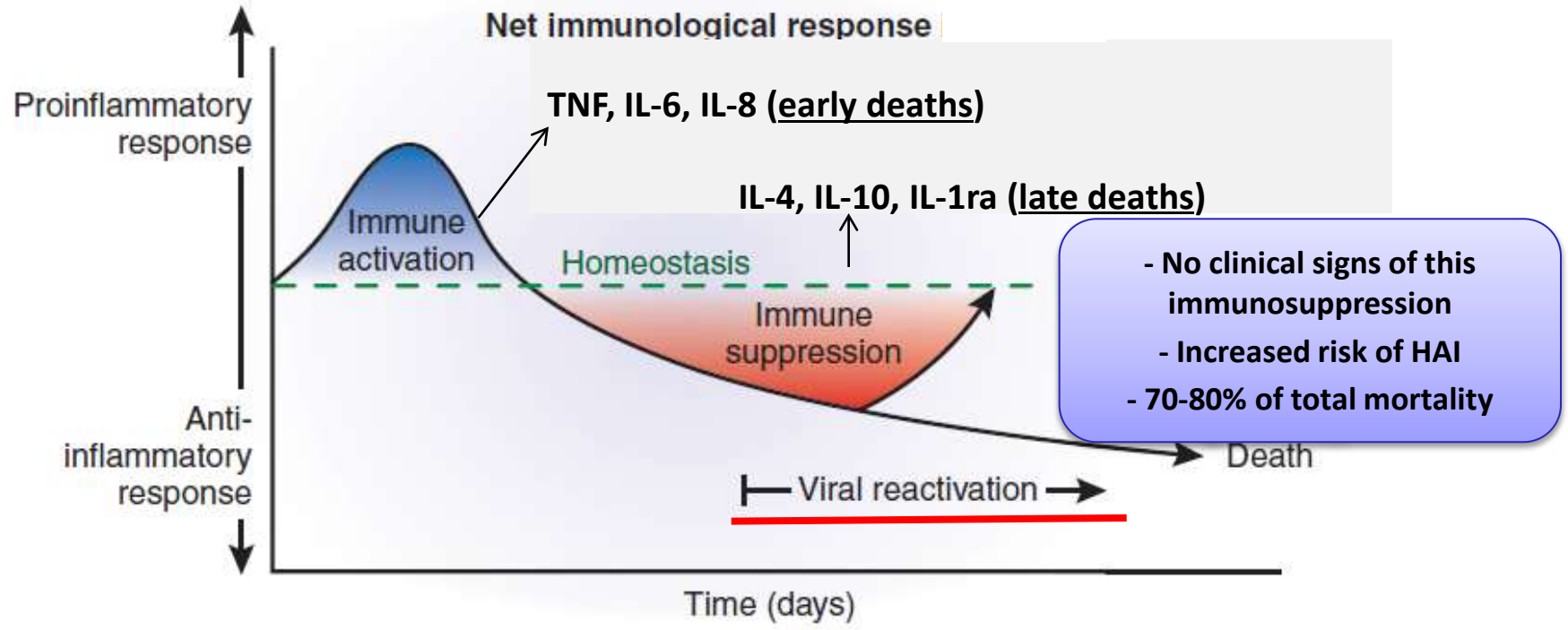
THE KEY QUESTION:

Would an early treatment applied within the first days post ICU admission be able to avoid many sepsis episodes, save thousands of dollars/euros and keep the patient alive at the end?



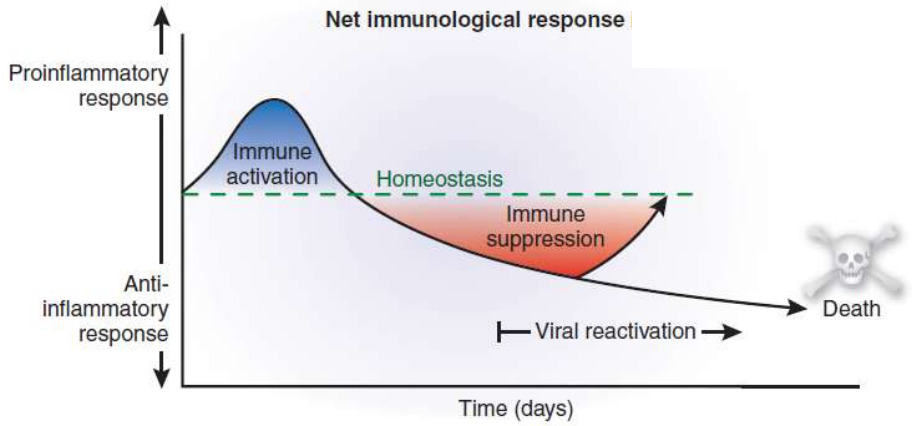
Burns: a sepsis-like syndrome!

Hyperinflammation followed by severe immunosuppression



Hotchkiss et al. *Nat Med* 2009

The Blood purification concept in burns



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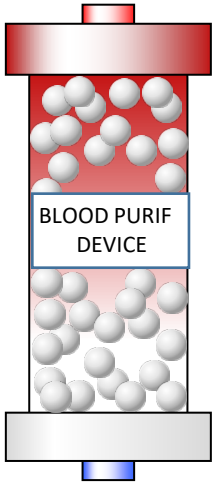

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Improved outcome ?

Extracorporeal blood purification techniques available in 2025

HEMOADSORPTION (Sorbents)

PMX-B (Toray/Estor)
Cytosorb (Cytosorbents)
LPS adsorber (Alteco)
HA330, HA380 (Jafron)
CA330（Jafron）
MG350 (Biosun)

CRRT filters

high adsorptive hemofiltration (oXiris, Baxter – PMMA, Toray)

high cut-off membranes (Emic2, Fresenius Medical Care)

NEW BLOOD PURIFICATION THERAPIES

(capable of leukocyte or bacteria or virus removal)

Seraph® (Exthera Medical)
FcMBL protein (Opsonix)
Hemopurifier® (Aethlon Medical)
other selective cytapheresis technology…

MISCELLANEOUS, OTHER TECHNIQUES

High-volume hemofiltration/Cascade hemofiltration/Pulse HVHF

Plasma exchanges

Coupled Plasma Filtration Adsorption

Outline

1) Severe burns: the classic clinical story

2) <u>Hemoadsorption in burn patients: what is the evidence?</u>

Available online at www.sciencedirect.com
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journal homepage: www.elsevier.com/locate/burns

Review

Extracorporeal blood purification in burns: A review

Katharina Linden [a,*], *Ian J. Stewart* [b], *Stefan F.X. Kreyer* [a], *Vittorio Scaravilli* [a], *Jeremy W. Cannon* [b,c], *Leopoldo C. Cancio* [a,d], *Andriy I. Batchinsky* [a], *Kevin K. Chung* [a,c]

[a] U.S. Army Institute of Surgical Research, Fort Sam Houston, San Antonio, TX 78234, United States
[b] San Antonio Military Medical Center, Fort Sam Houston, San Antonio, TX 78234, United States

Literature is extremely scarce when it comes to HA + burns

Table 1 – Examples, technical details, and studies for a selection of membranes designed for cytokine removal.

Name	SepteX® Gambro	oXiris® Gambro	PMMA different Toray membranes	Polymyxin B Toraymyxin®, Toray	CytoSorb® CytoSorbents	CPFA® Bellco
Type	High cutoff membrane	Adsorptive membrane	Adsorptive membrane	Adsorptive membrane	Adsorbing column	Coupled plasma filtration and adsorption
Use	As CRRT in sepsis manufacturer recommends CVVHD; study planned in CVVH	As CRRT in sepsis Use in CVVH or CVVHDF modes	As CRRT In different modes	Sepsis/endotoxemia hemoperfusion	Cytokine hemoperfusion	In multi-organ failure and/or sepsis CPFA
Fibers	Polyarylether-sulfon	Acrylonitril + natrium-methallyl-sulfonat-copolymer + polyethylenimin	Polymethylmetha-crylate	Polymyxin B covalently immobilized; polystyrene derived	Cross-linked divinylbenzene/ polyvinylpyrrolidone beads	Reverse-phase styrenic polymer resin
Surface	1.1 m^2	1.5 m^2	1–2.1 m^2	N/A	850 m^2/g	600–800 m^2/g
Studies/reviews in burn patients	N/A Might play a role in removing myoglobin [2,23]	N/A	Case report [44] reduction of IL-6	Reduction of endotoxin, IL-1ß, IL-6, IL-8, and TNF-α; no different outcomes compared to no treatment [41]	N/A Might be able to remove myoglobin	N/A
Studies/reviews in septic patients	Greater relative decrease of IL-6 than with high-flux membrane [54] Preliminary results of HICOSS no difference in mortality, duration of ICU-stay, need of catecholamines compared to conventional CVVHD membrane [2]	No studies in humans	Removed cytokines ef-fectively and improved hemodynamics (CHDF mode) [43]	EUPHAS: improved hemodynamics, organ dysfunction, 28-day mortality in intra-abdominal Gram-negative infections [38]	CytoSorb's European Sepsis Trial: reduction in IL-6, MCP-1, IL-1ra and IL-8. No IL-10, 28-day, and 60-day mortality reduction. No removal of endotoxin [51]	Improved hemodynamics (CPFA + HD) compared to CVVHDF; may restore leukocyte responsiveness [58]

Linden et al. *Burns* 2014

Burn pigs

15 pigs

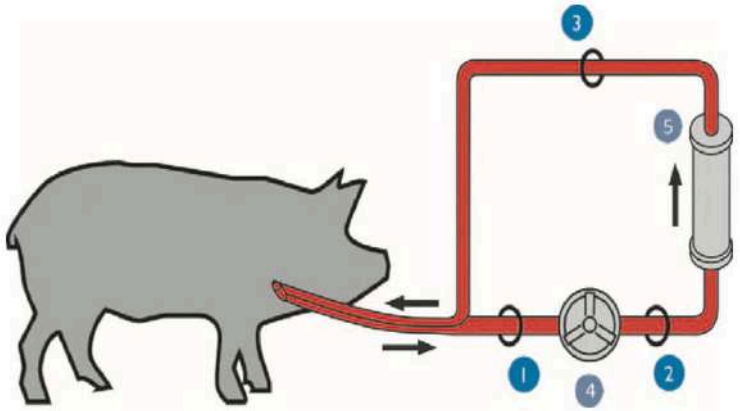
40% TBSA

9 pigs HA vs 6 sham

SHOCK, Vol. 44, No. 5, pp. 487–495, 2015

EVALUATION OF THE CYTOSORB™ HEMOADSORPTIVE COLUMN IN A PIG MODEL OF SEVERE SMOKE AND BURN INJURY

Katharina Linden,[*§] Vittorio Scaravilli,[*¶] Stefan F.X. Kreyer,[*‖] Slava M. Belenkiy,[*] Ian J. Stewart,[‡] Kevin K. Chung,[*†] Leopoldo C. Cancio,[*†] and Andriy I. Batchinsky[*]



6-hour HA session or sham session at day 1 day 2 and day 3

Serum cytokines (IL-1b, IL-6, IL-8, IL-10, TNF-alpha) were measured

- **systemically,**
- **locally in bronchoalveolar lavage fluid**
- **in circulating blood before and after the adsorbing column to evaluate single pass clearance by the device.**

Linden et al. *Shock* 2015

Significant removal of IL 1b, IL 6, IL 10 et myoglobine (from 25% to 40%) by the device but no significant systemic or pulmonary cytokine reductions

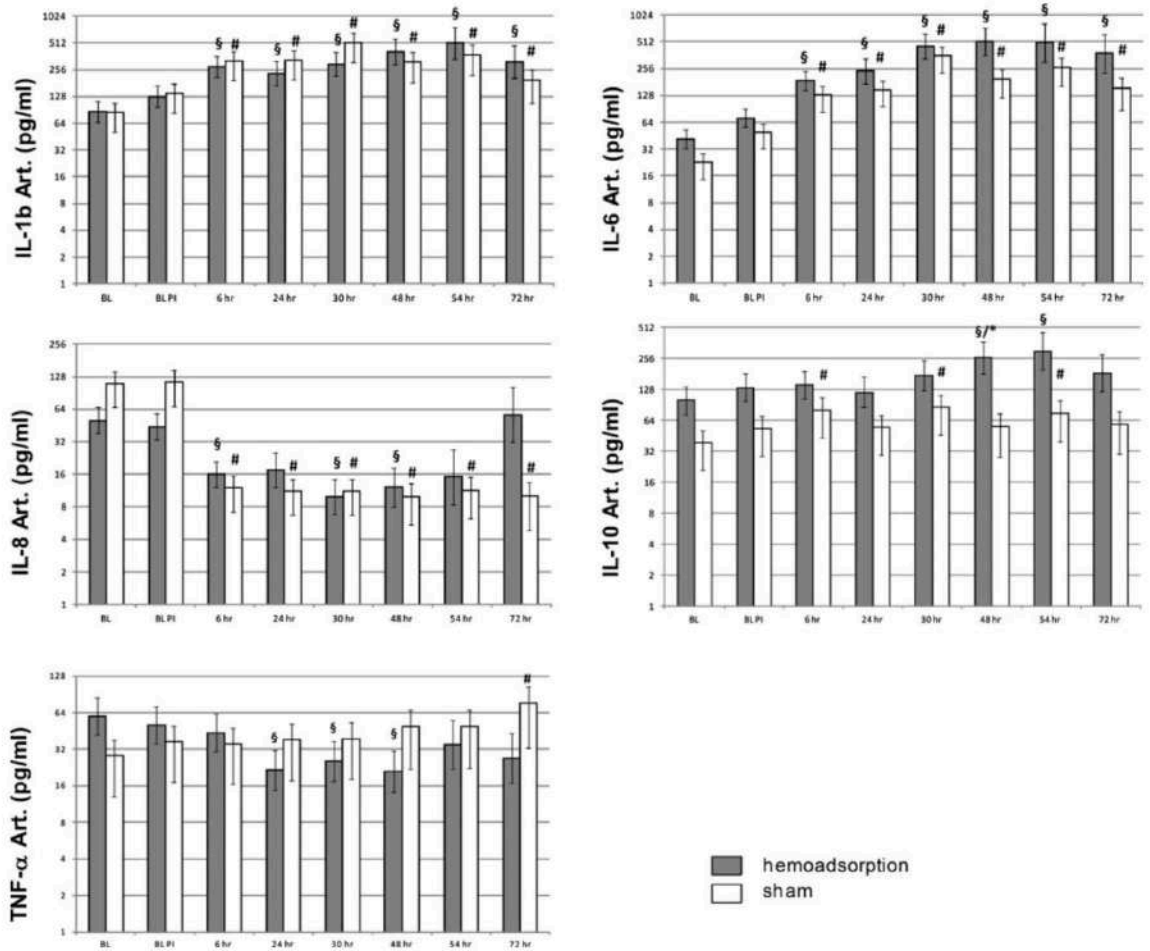


FIG. 2. **Effect of hemoadsorption on systemic cytokine concentrations measured in serum samples (mean ± SEM, pg/mL).** Each panel shows a different cytokine. BL, baseline; PI, post-injury. § = $P < 0.05$ compared with BL hemoadsorption, # = $P < 0.05$ compared with BL sham, * = $P < 0.05$ compared with sham same timepoint.

Linden et al. *Shock* 2015

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journal homepage: www.elsevier.com/locate/burns

CytoSorb® in burn patients with septic shock and Acute Kidney Injury on Continuous Kidney Replacement Therapy is associated with improved clinical outcome and survival

Filippo Mariano [a,b,*], *Domenico Greco'* [a], *Nadia Depetris* [c], *Alberto Mella* [a,b], *Alberto Sciarrillo* [d], *Maurizio Stella* [d], *Maurizio Berardino* [c], *Daniela Risso* [d], *Roberto Gambino* [b,e], *Luigi Biancone* [a,b]

[a] *Nephrology, Dialysis and Transplantation U, Department of General and Specialized Medicine, City of Health and Science, CTO Hospital, Turin, Italy*
[b] *Department of Medical Sciences, University of Turin, Turin, Italy*
[c] *Anesthesia and Intensive Care 3, Department of Anesthesia and Intensive Care, City of Health and Science, CTO Hospital, Turin, Italy*
[d] *Plastic Surgery and Burn Center, Department of General and Specialized Surgery, City of Health and Science, CTO Hospital, Turin, Italy*
[e] *Laboratory of Diabetology and Metabolism, University of Turin, Italy*

Retrospective analysis of 35 burn patients who received CRRT for septic shock-associated AKI
- 11 patients : CRRT + HA
- 24 patients : CRRT only

Mariano et al. Burns 2024

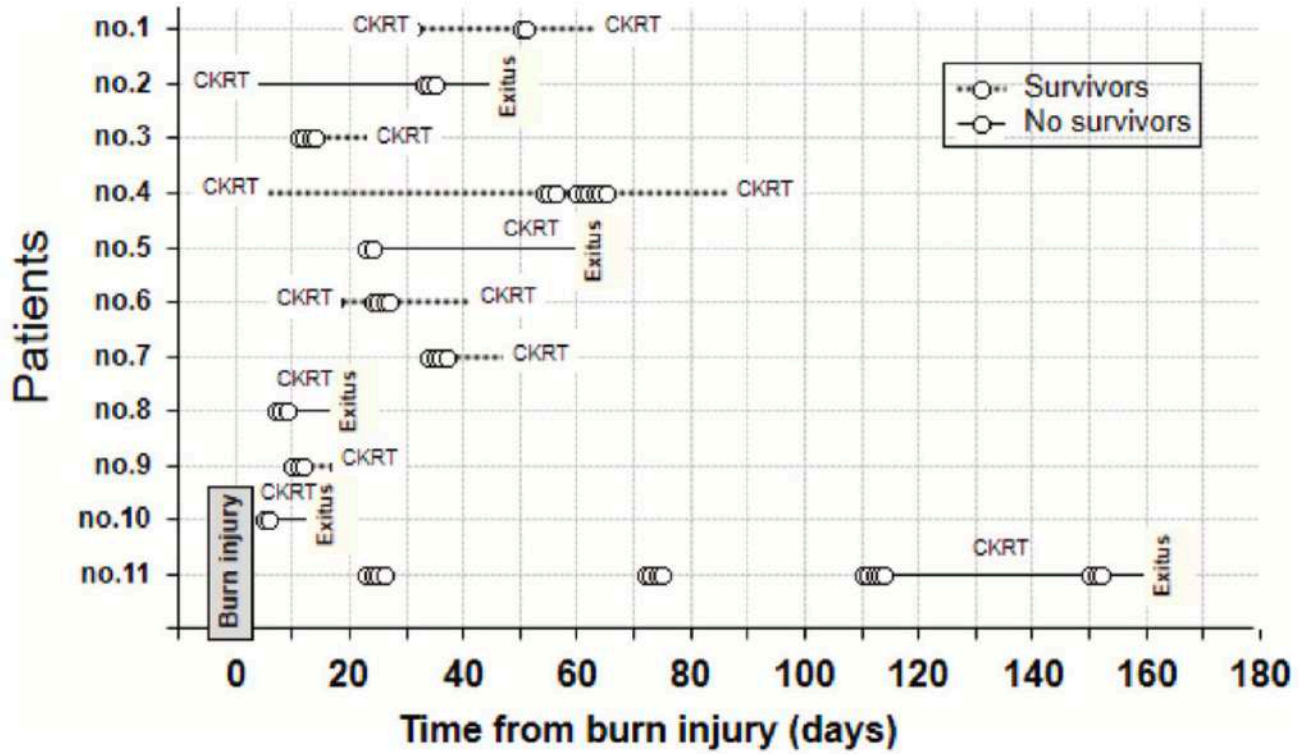


Fig. 1 – Timing of application of CRRT and CytoSorb® in the Sorbent group. The figure shows the ICU mortality and the detailed outcome of the 11 treated patients.

Mariano et al. Burns 2024

Table 2 – Baseline characteristics of 11 septic shock burn patients on CRRT treated with CytoSorb® (Sorbent group) and 24 burn septic shock patients treated with only CRRT [a] (Control group).

	Sorbent group	Control group	p
Patients (n)	11	24	——
In-hospital mortality (%, n)	45.4%, 5	70.8%, 17	0.143
Age (years)	63.0 (43.0-78.0)	72.0 (49.0-79.0)	0.647
Total body surface area (%)	35.0 (15.0-50.0)	35.0 (20.0-60.0)	0.634
Revised Baux score	115.8 (103.0-139.3)	116.4 (101.2-141.2)	0.452
Baux index expected mortality	54.0 (30.2-87.8)	55.1 (27.4-89.3)	0.749
Gender ratio (male/female)	8/3	20/4	0.381
Septic shock (%, n)	100%, 11	91.7%, 22	0.334
Mechanical ventilation (%, n)	100%, 11	87.5%, 21	0.309
CRRT start interval (days from admission)	10 (5-23)	8.5 (2-19.5)	0.716
Patients survival (days from CRRT /Cytosorb start)	46 (18-47)	11 (7-32)	0.132
Recovery from CRRT (%, n)	54.5%, 6	29.2%, 7	0.154
CRRT duration (days)	26 (15-46)	11 (7-26)	0.250
Citrate anticoagulation (%, n)	100%, 11	87.5%, 21	0.309
Diuresis (at 1st day of CRRT)	560 (120-2150)	385 (115-1350)	0.566
SOFA score[b] (at 1st day of CRRT)	12 (11-12)	12 (11-13)	0.839
Lactate (mmol/L, at 1st day of CRRT)	1.7 (1.5-3.0)	2.0 (1.5-3.6)	0.369
Norepinephrine (ug/Kg/min, at 1st day of CRRT)	0.50 (0.20-0.80)	0.35 (0.20-0.55)	0.115

Data are given as median (the 25th and 75th percentiles) or as percentage when appropriate. Student T-test or Fisher's exact test was done when appropriate

[a] CKRT = Continuous Kidney Replacement Therapy

[b] SOFA score = Sequential Organ Failure Assessment score

Mariano et al. Burns 2024

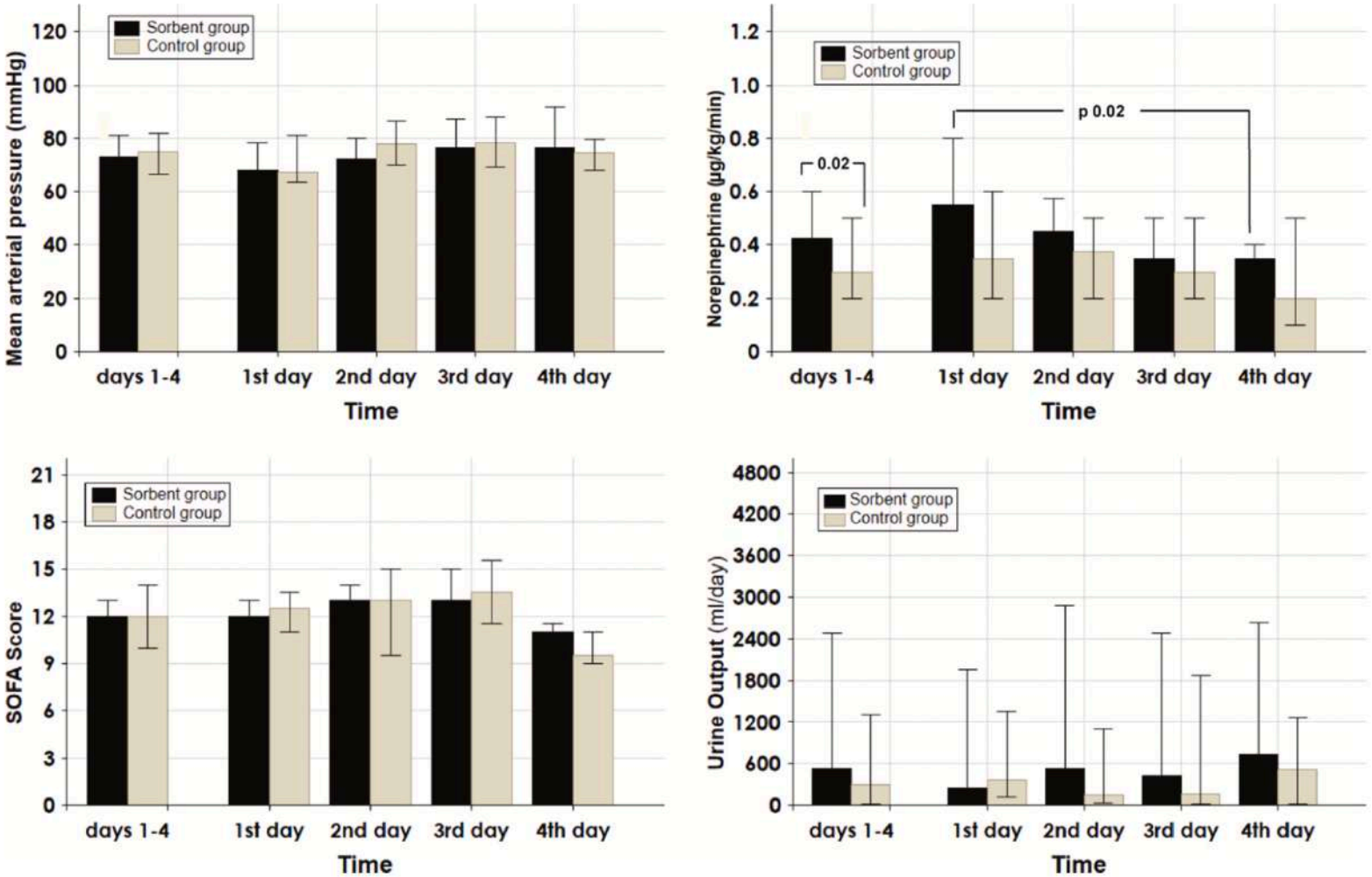
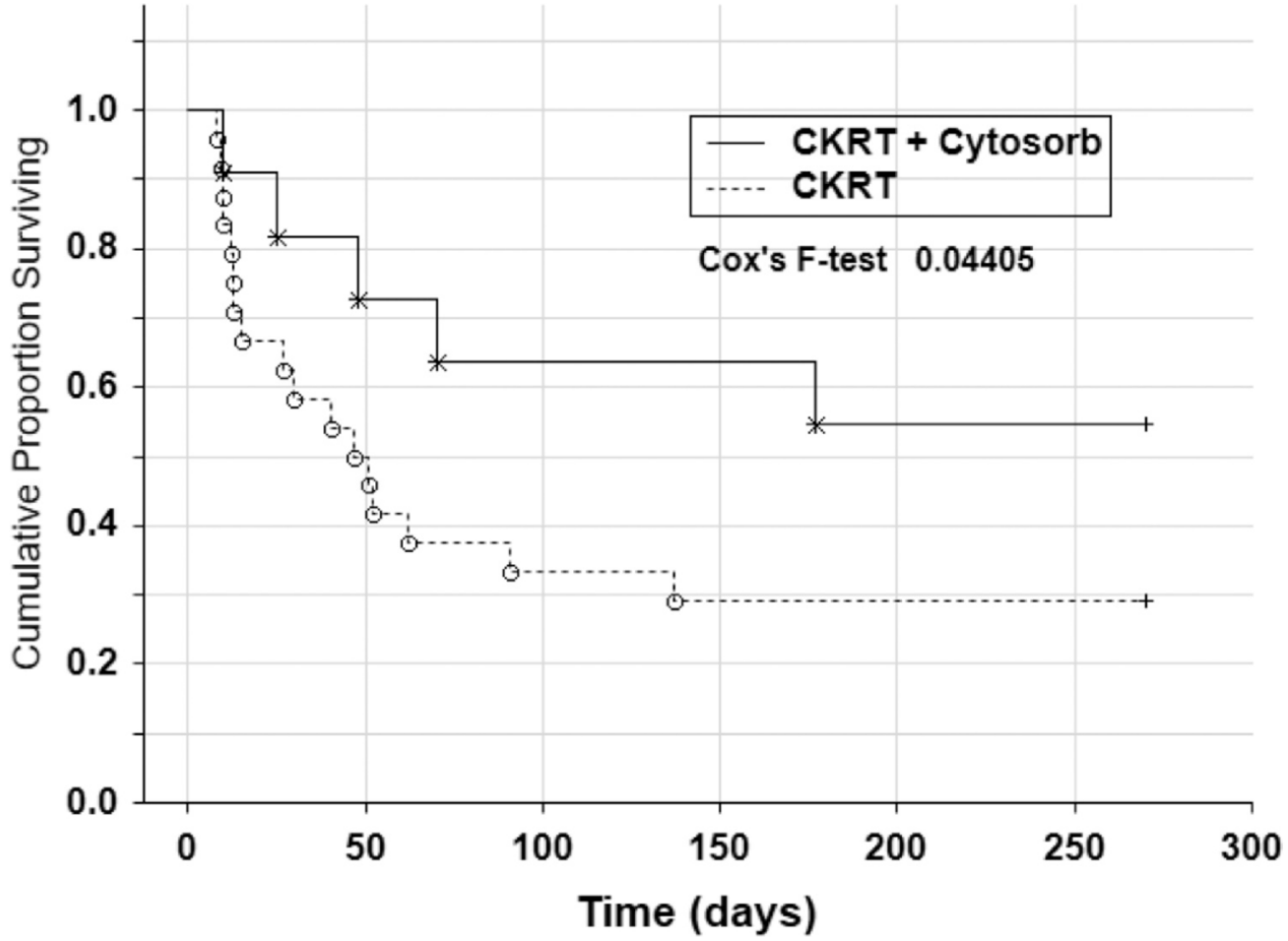


Fig. 4 – Outcome of MAP, norepinephrine requirement, SOFA score and Urine Output in the first 4 days for Sorbent (n 11 patients) and Control groups (n 24 patients). A significant difference was found between the norepinephrine requirement of days 1–4 and between day 1 and day 4 for patients of the Sorbent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

Mariano et al. Burns 2024



In hospital mortality
CRRT + HA : 45%
CRRT : 70%

Fig. 2 – Survival analysis by Kaplan-Meyer curves for Sorbent and Control groups. The figure shows the in-hospital mortality encompassing the period of ICU stay, ward stay, and rehabilitation for the Sorbent (n 11 patients) and Control groups (n 24 patients).

Mariano et al. Burns 2024

Study discussion

- HA was given here more for sepsis than for the burn shock!

- HA was given late (in a very heterogeneous way), when AKI occurs, after a few days post ICU admission

CONCLUSION

- **Burns: sepsis-like syndrome with complex pathophysiology**

- **Hemoadsorption in burns: very limited data available but promising**

- **Strong rationale to deeply assess hemoadsorption in burns**