



Epuration et sepsis



Pr Olivier JOANNES-BOYAU

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Liens d'intérêts

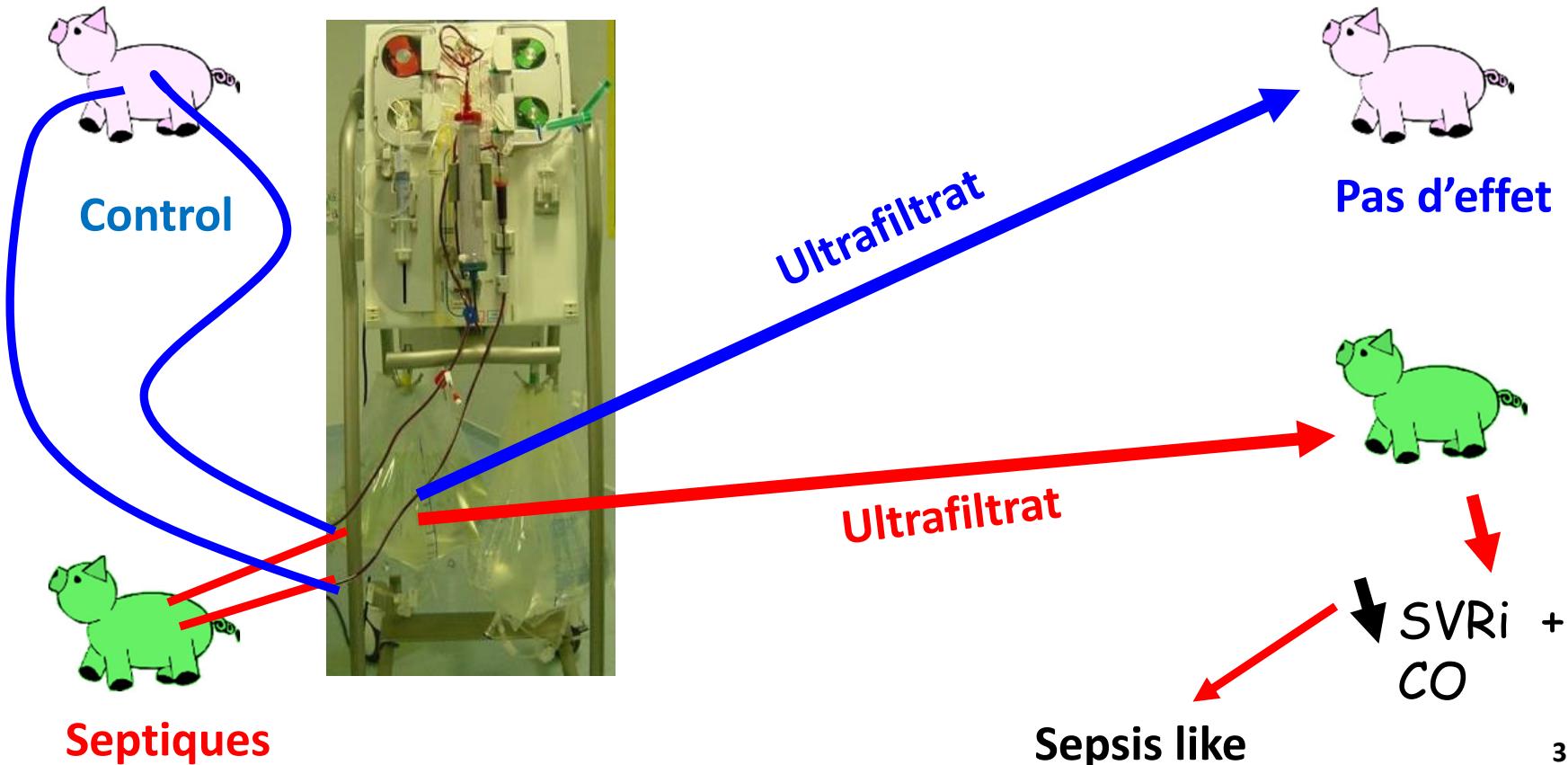




Infusion of ultrafiltrate from endotoxemic pigs depresses myocardial performance in normal pigs

1993

Albert F. Grootendorst, Eric F.H. van Bommel, Leo A.M.G. van Leengoed, Arthur R.H. van Zanten, Herman J.C. Huipen, A.B. Johan Groeneveld

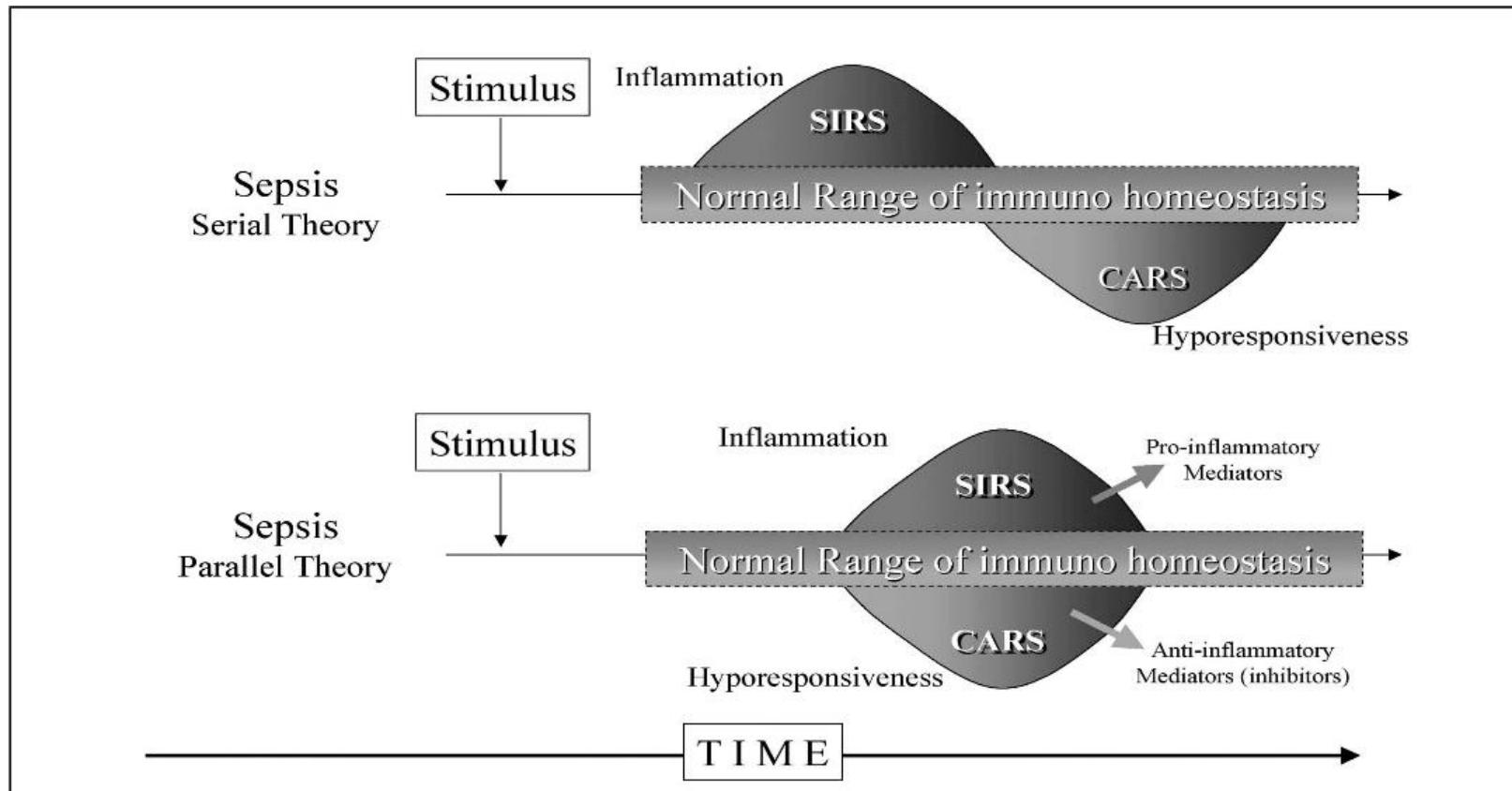




Interpreting the Mechanisms of Continuous Renal Replacement Therapy in Sepsis: The Peak Concentration Hypothesis

Claudio Ronco, *Ciro Tetta, †Filippo Mariano, *Mary Lou Wratten, *Monica Bonello

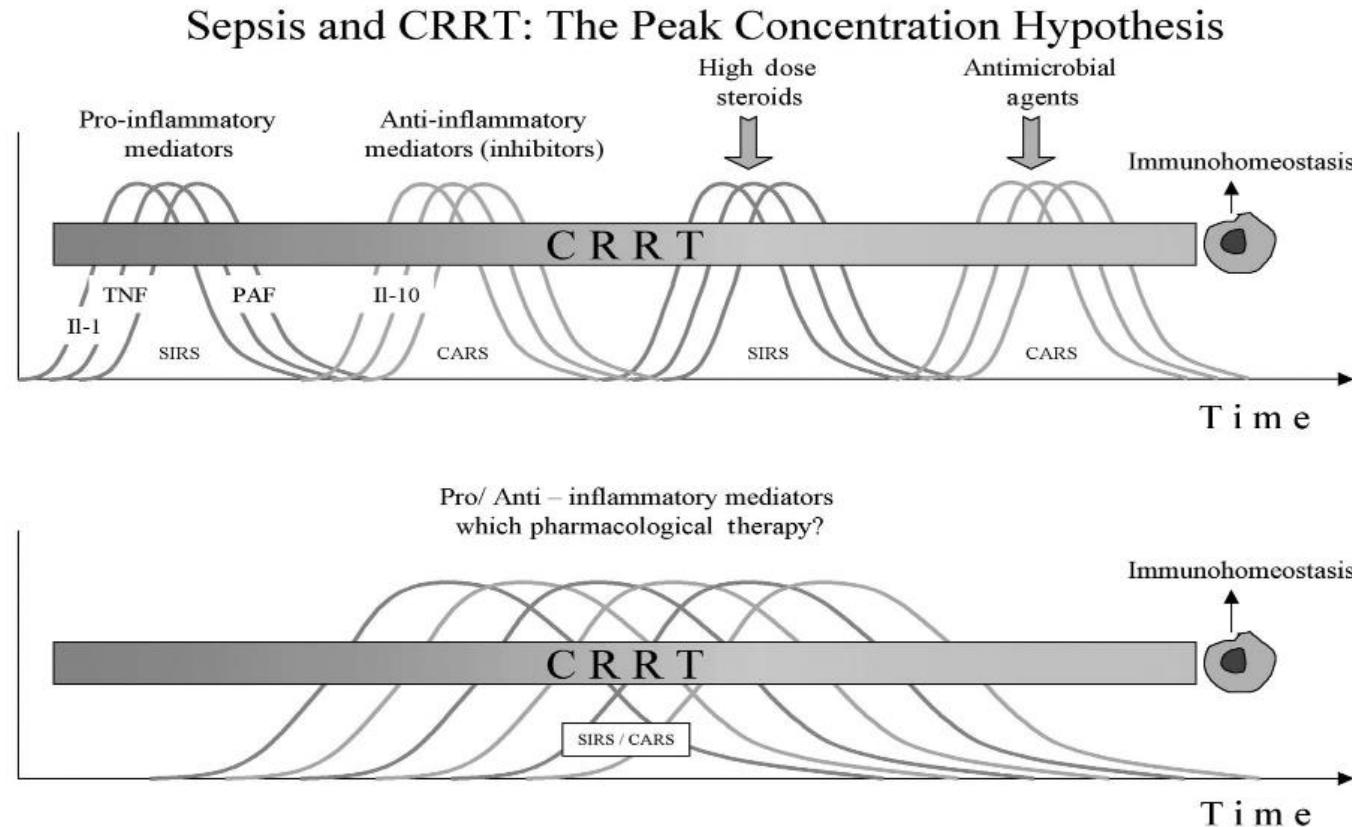
2003



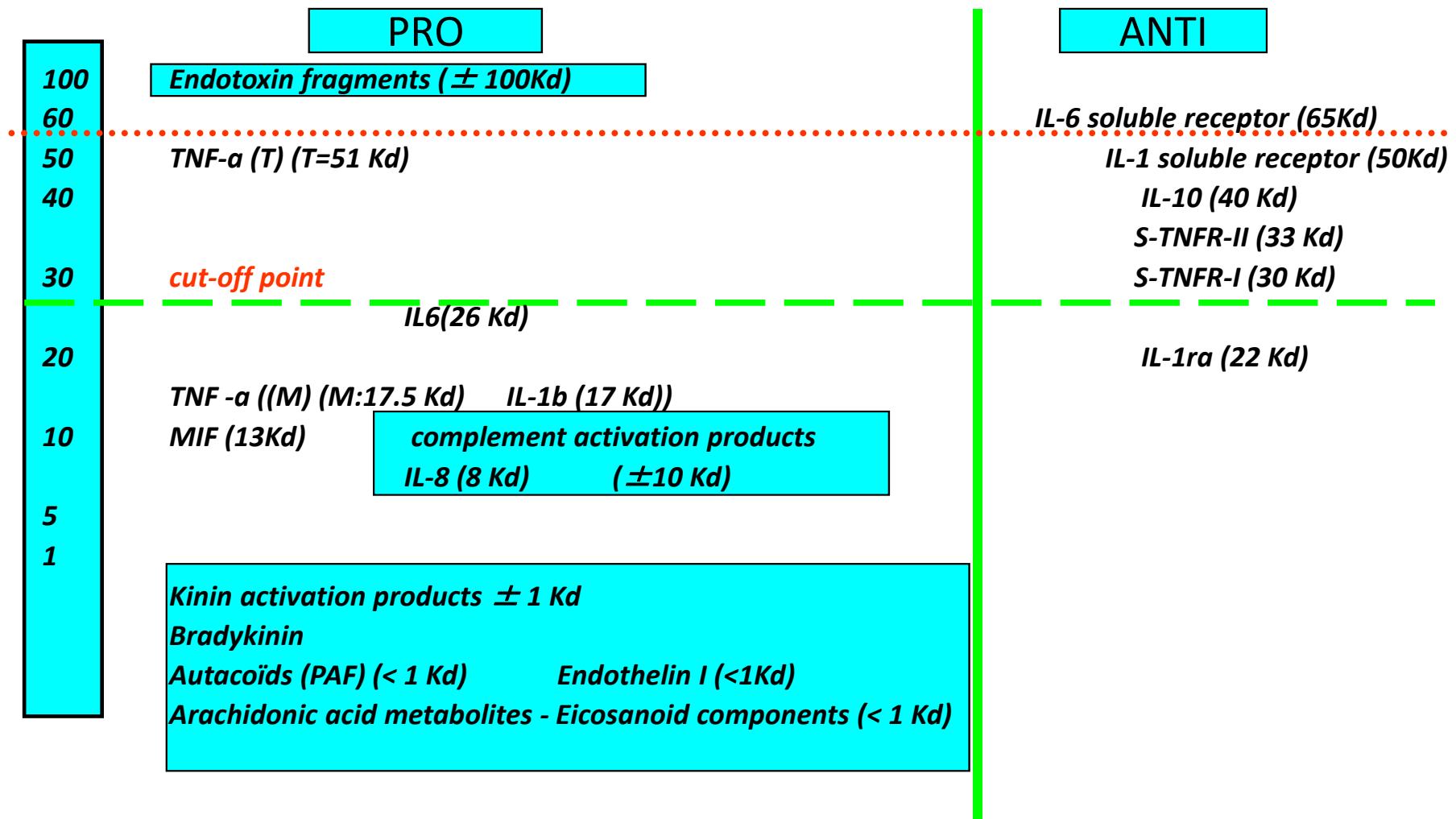
Interpreting the Mechanisms of Continuous Renal Replacement Therapy in Sepsis: The Peak Concentration Hypothesis

Claudio Ronco, *Ciro Tetta, †Filippo Mariano, *Mary Lou Wratten, *Monica Bonello

2003



Filtration des Cytokines

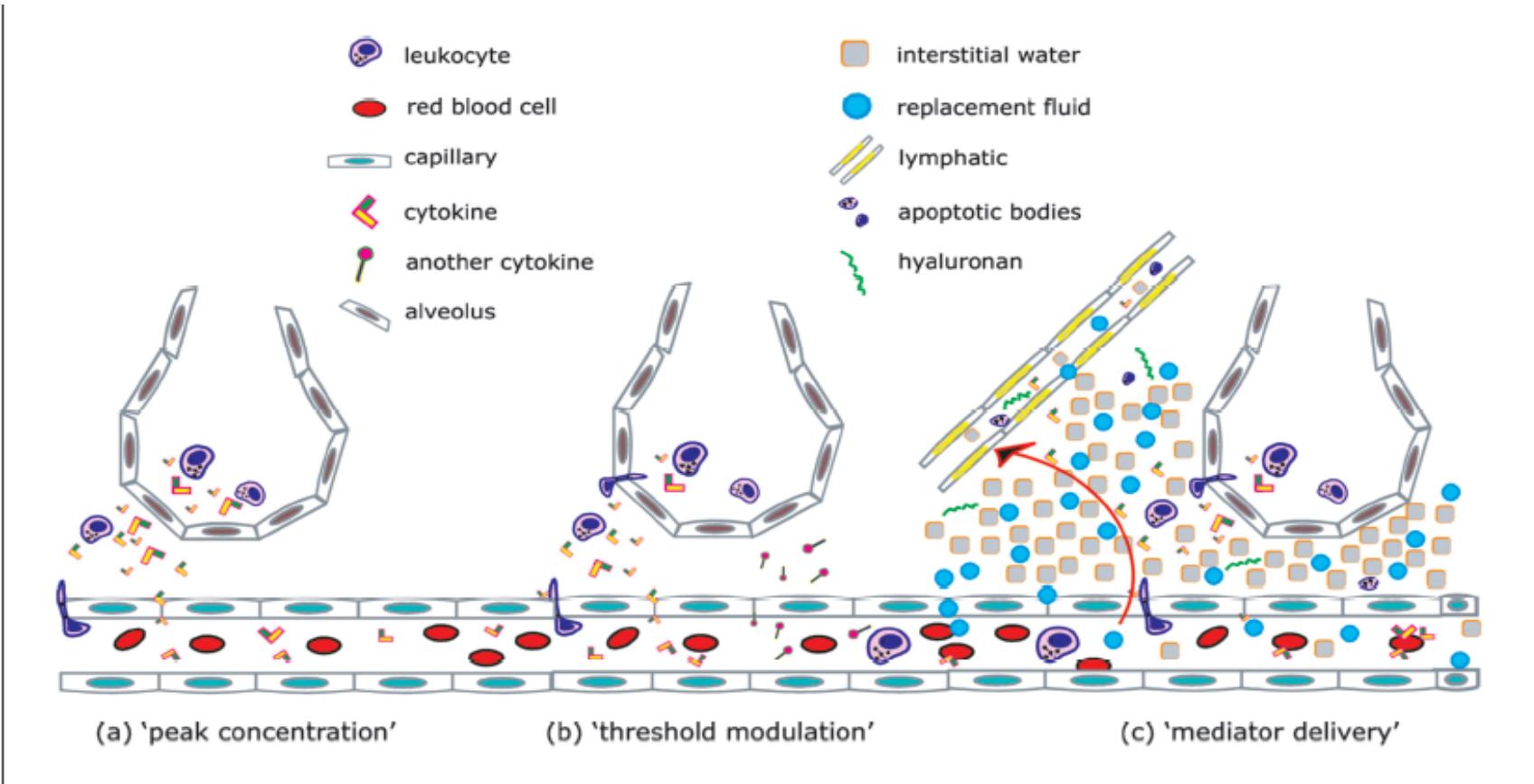




Hemofiltration for cytokine-driven illnesses: The mediator delivery hypothesis

J.V. DI CARLO¹, S.R. ALEXANDER²

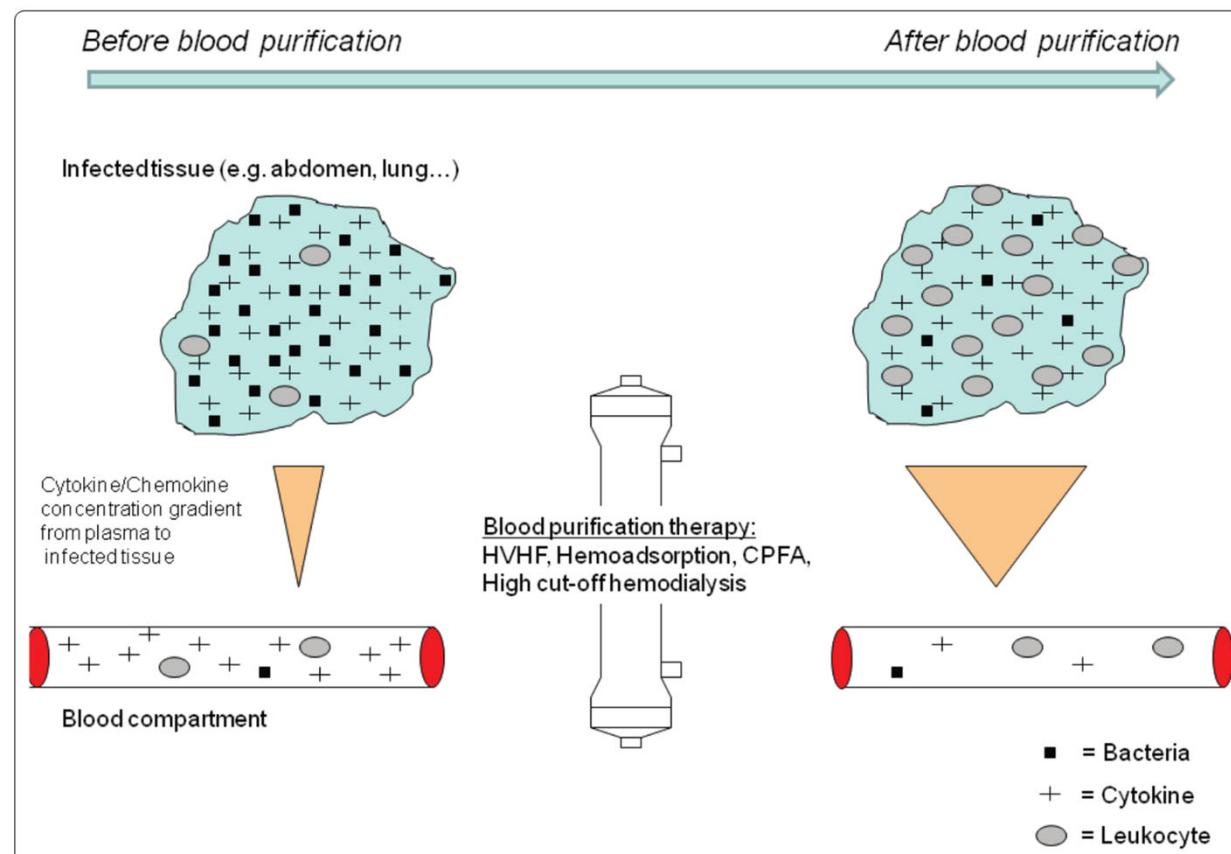
2005



Modulation of chemokine gradients by apheresis redirects leukocyte trafficking to different compartments during sepsis, studies in a rat model

2014

Zhi-Yong Peng^{1,2}, Jeffery V Bishop², Xiao-Yan Wen^{1,2}, Michele M Elder^{1,2}, Feihu Zhou^{1,2}, Anan Chuasawan^{1,2}, Melinda J Carter², Jason E Devlin³, A Murat Kaynar^{1,2}, Kai Singbartl^{1,2}, Francis Pike^{1,2}, Robert S Parker^{1,2,5,6}, Gilles Clermont^{1,2,5,6}, William J Federspiel^{1,2,4,6} and John A Kellum^{1,2,4,6,7*}



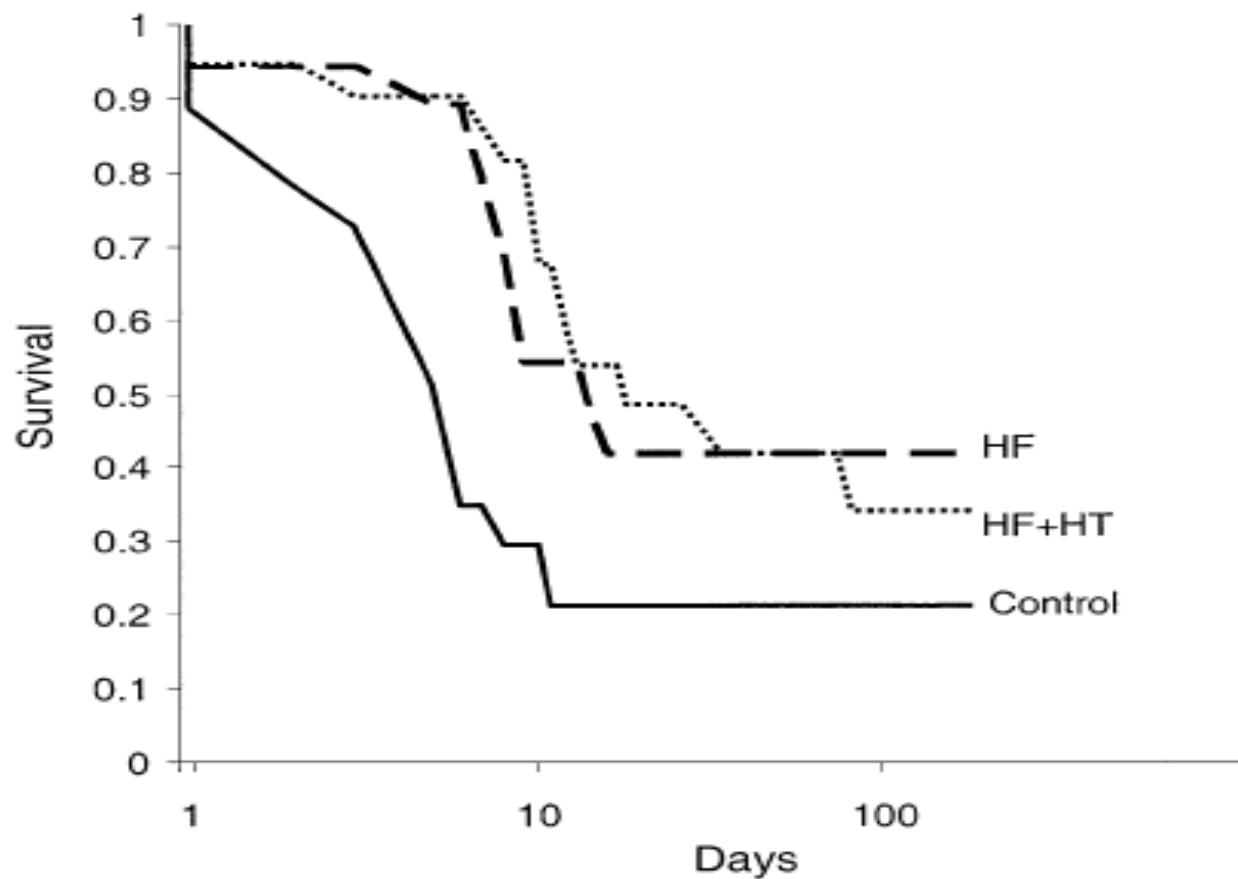
Le volume ?

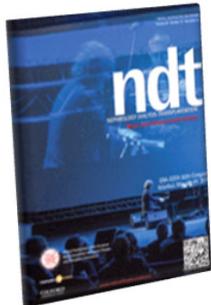


High-Volume Hemofiltration After Out-of-Hospital Cardiac Arrest

Ivan Laurent, MD,* Christophe Adrie, MD,† Christophe Vinsonneau, MD,* Alain Cariou, MD,*
Jean-Daniel Chiche, MD,* Alice Ohanessian, MD,‡ Christian Spaulding, MD,‡ Pierre Carli, MD,§
Jean-François Dhainaut, MD, PhD,* Mehran Monchi, MD*

2005

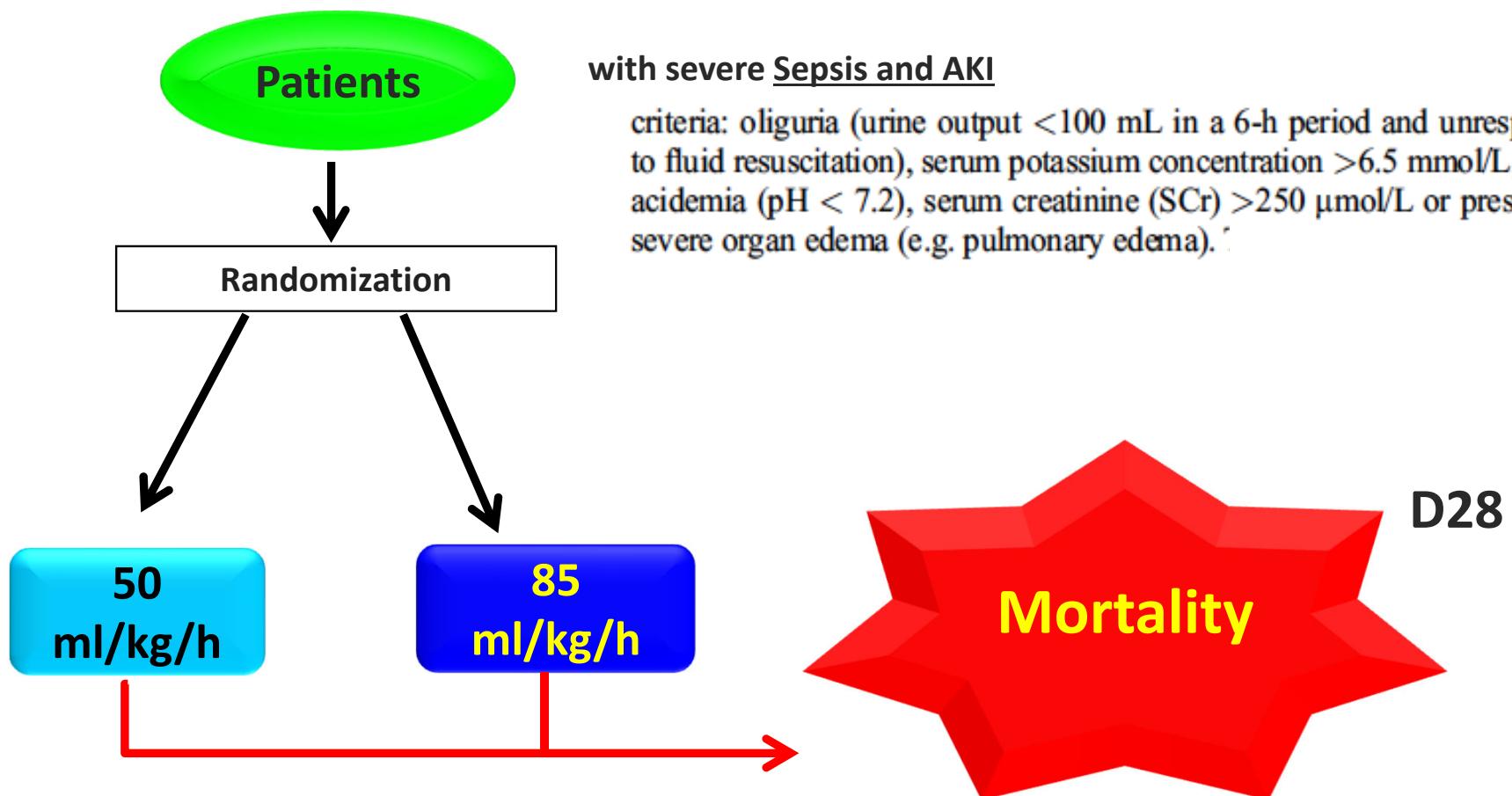


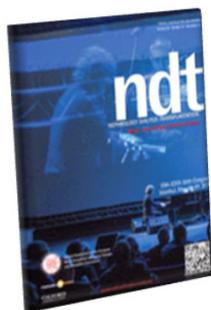


Effect of the intensity of continuous renal replacement therapy in patients with sepsis and acute kidney injury: a single-center randomized clinical trial

Ping Zhang¹, Yi Yang¹, Rong Lv¹, Yuntao Zhang², Wenqing Xie¹ and Jianghua Chen¹

(2012)

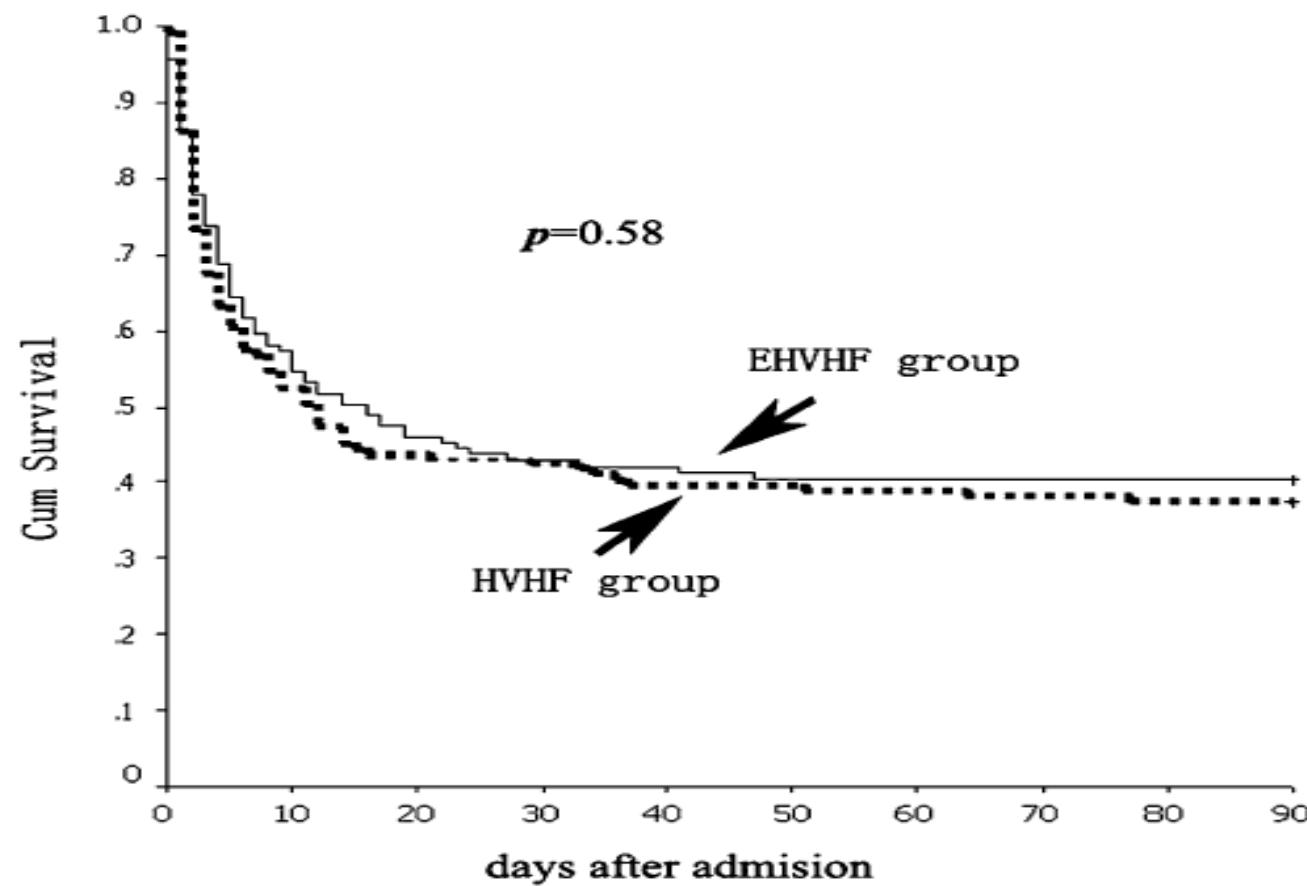




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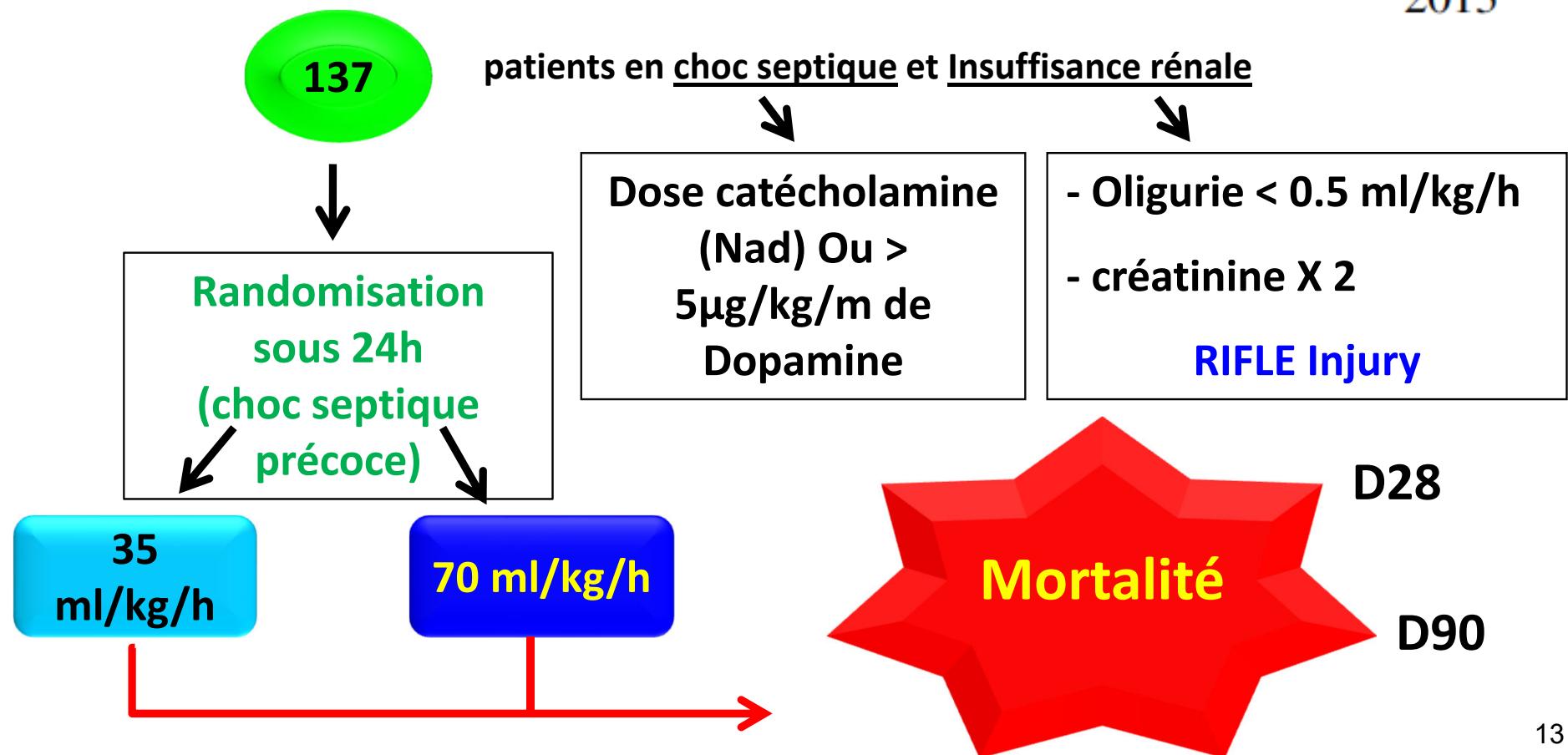




High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial

Olivier Joannes-Boyau
Patrick M. Honoré
Paul Perez
Sean M. Bagshaw
Hubert Grand
Jean-Luc Canivet
Antoine Dewitte

2013

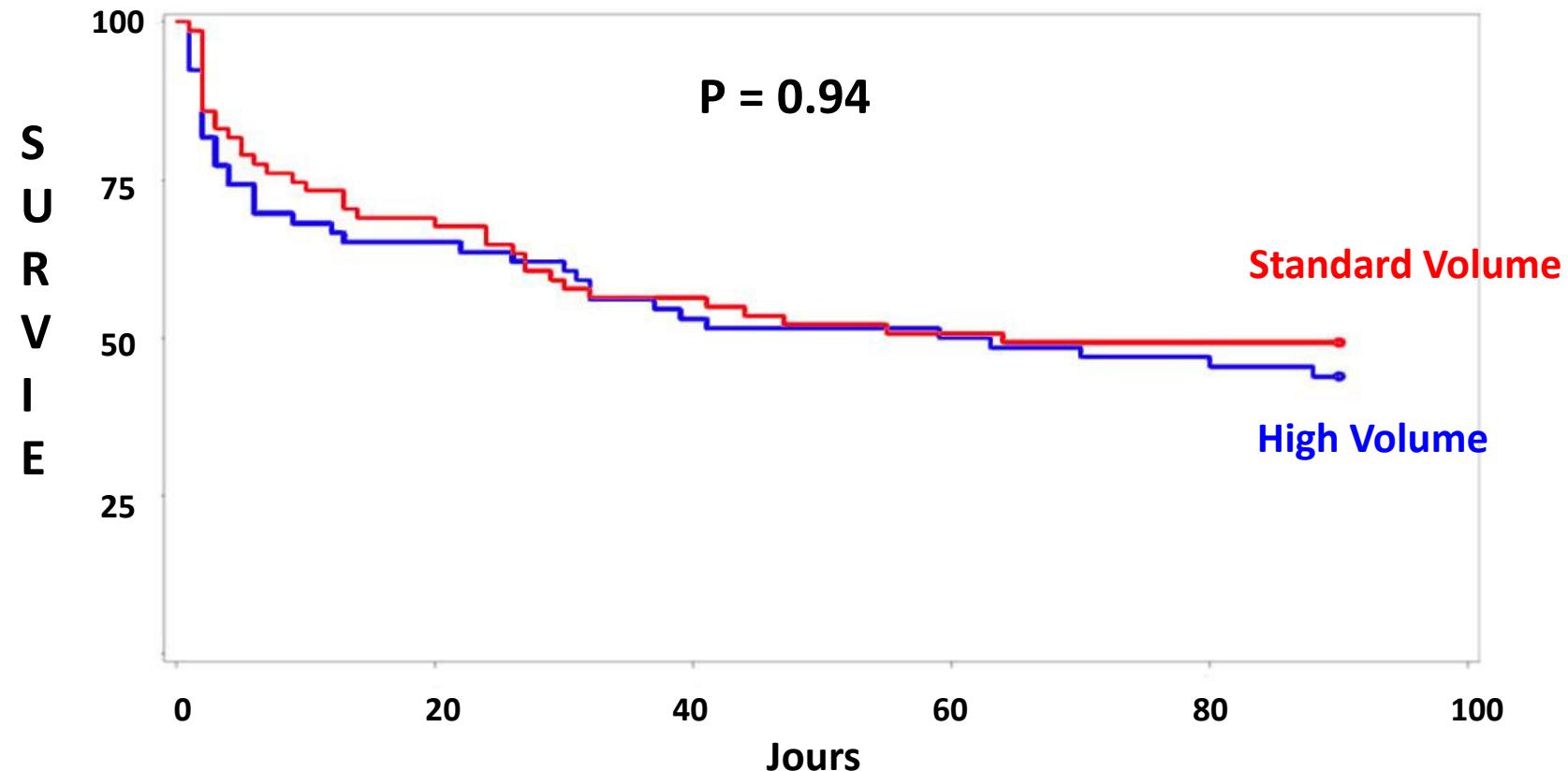




High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial

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Antoine Dewitte

2013



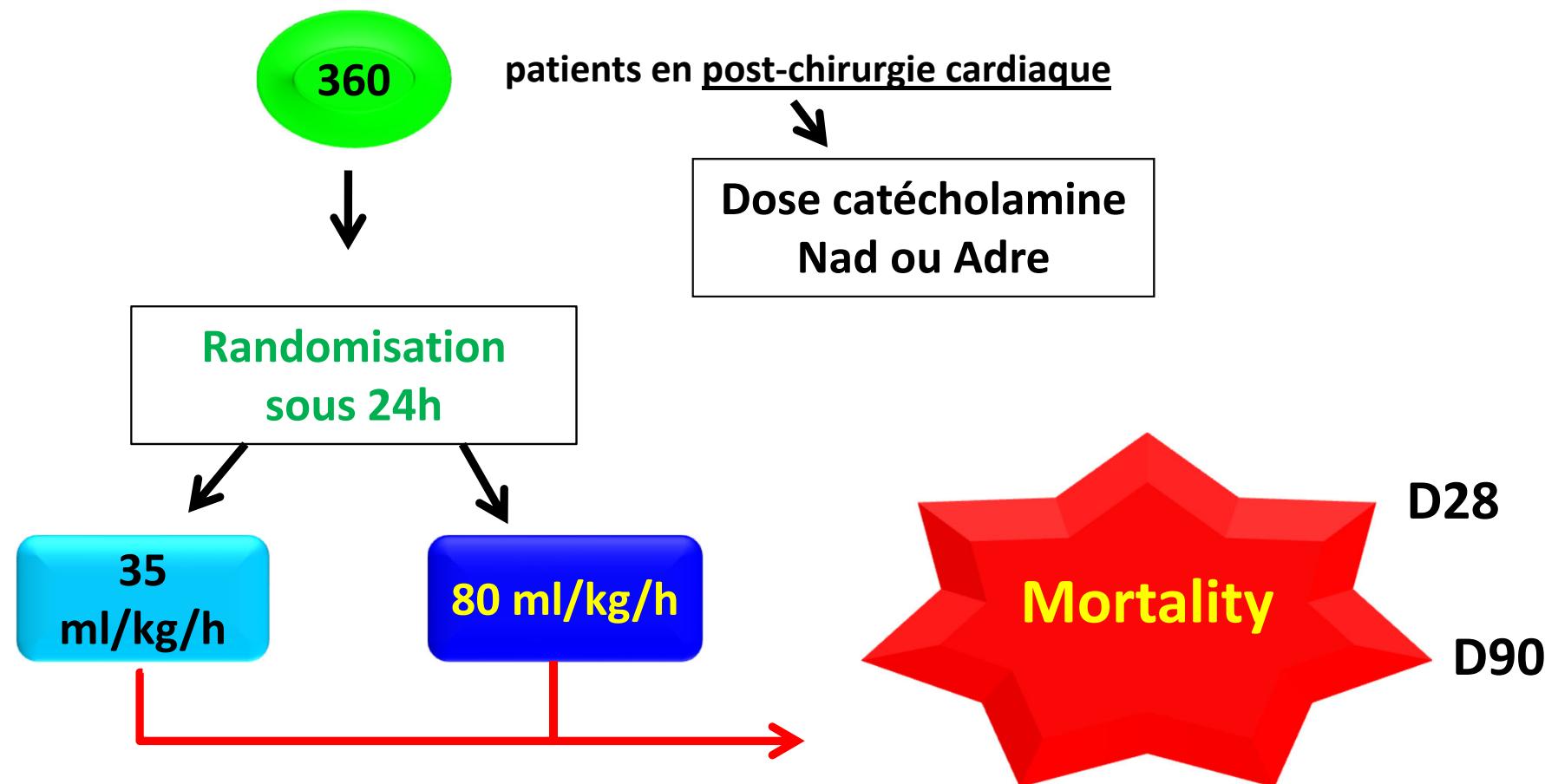


Early High-Volume Hemofiltration versus Standard Care for Post-Cardiac Surgery Shock

The HEROICS Study

Alain Combes¹, Nicolas Bréchet¹, Julien Amour², Nathalie Cozic³, Guillaume Lebreton⁴, Catherine Guidon⁵, Elie Zogheib⁶, Jean-Claude Thiranos⁷, Jean-Christophe Rigal⁸, Olivier Bastien⁹, Hamina Benhaoua¹⁰, Bernard Abry¹¹, Alexandre Ouattara¹², Jean-Louis Trouillet¹, Alain Mallet³, Jean Chastre¹, Pascal Leprince⁴, and Charles-Edouard Luyt¹

2015



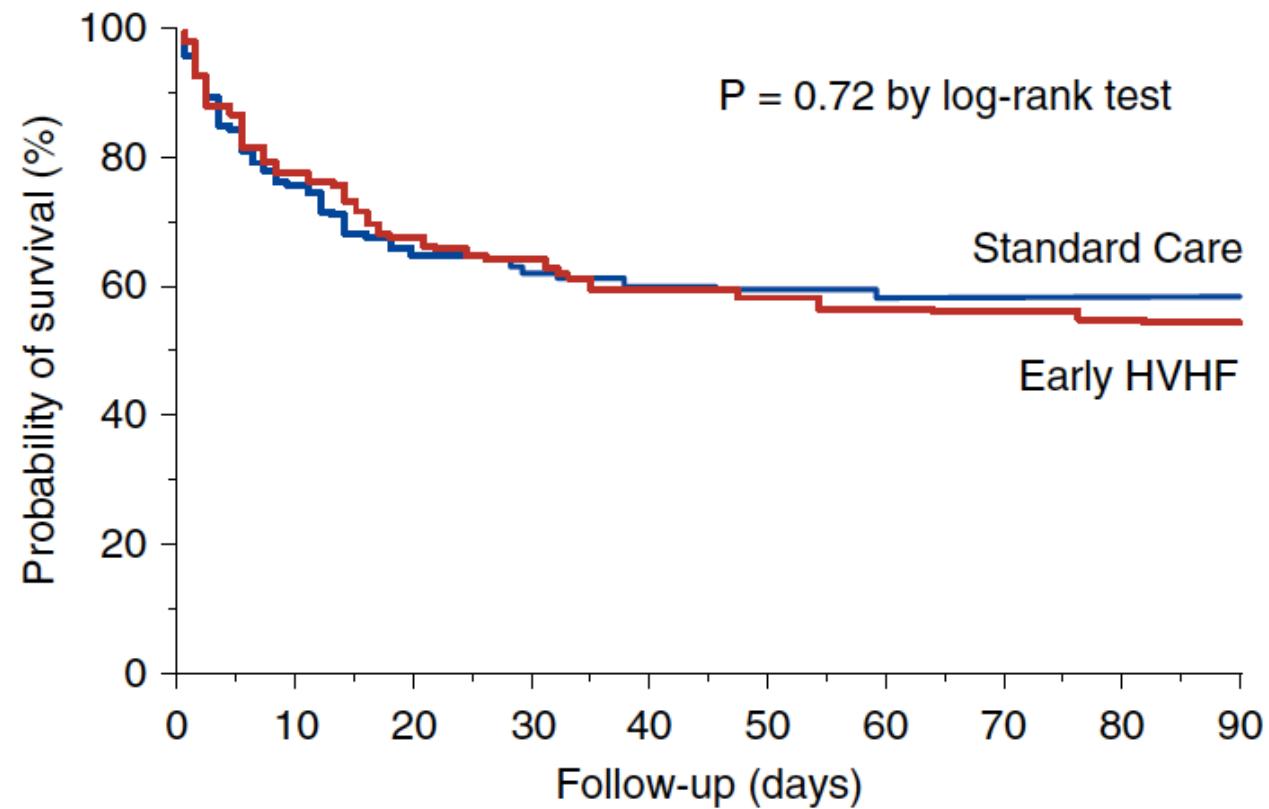


Early High-Volume Hemofiltration versus Standard Care for Post-Cardiac Surgery Shock

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Alain Combes¹, Nicolas Bréchot¹, Julien Amour², Nathalie Cozic³, Guillaume Lebreton⁴, Catherine Guidon⁵, Elie Zogheib⁶, Jean-Claude Thiranos⁷, Jean-Christophe Rigal⁸, Olivier Bastien⁹, Hamina Benhaoua¹⁰, Bernard Abry¹¹, Alexandre Ouattara¹², Jean-Louis Trouillet¹, Alain Mallet³, Jean Chastre¹, Pascal Leprince⁴, and Charles-Edouard Luyt¹

2015



Timing ?

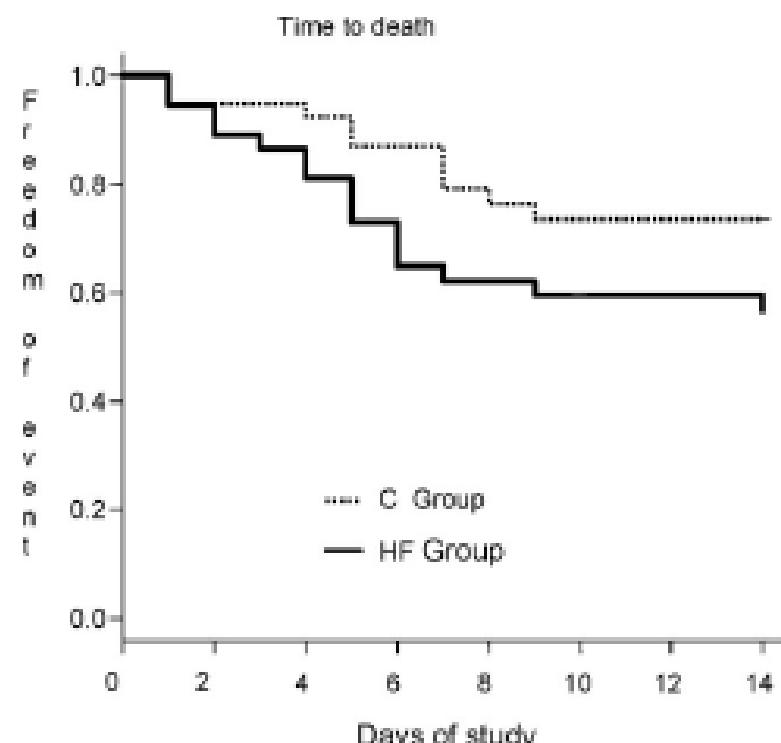
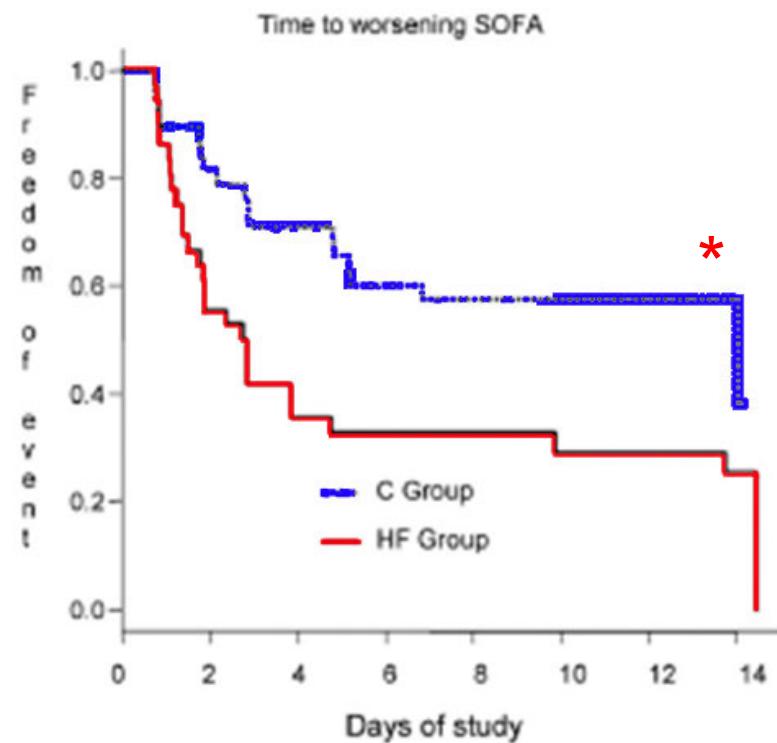




Impact of continuous venovenous hemofiltration on organ failure during the early phase of severe sepsis: A randomized controlled trial*

Didier Payen, MD, PhD; Joaquim Mateo, MD; Jean Marc Cavaillon, PhD; François Fraisse, MD; Christian Floriot, MD; Eric Vicaut, MD, PhD; for the Hemofiltration and Sepsis Group of the Collège National de Réanimation et de Médecine d'Urgence des Hôpitaux extra-Universitaires

2009





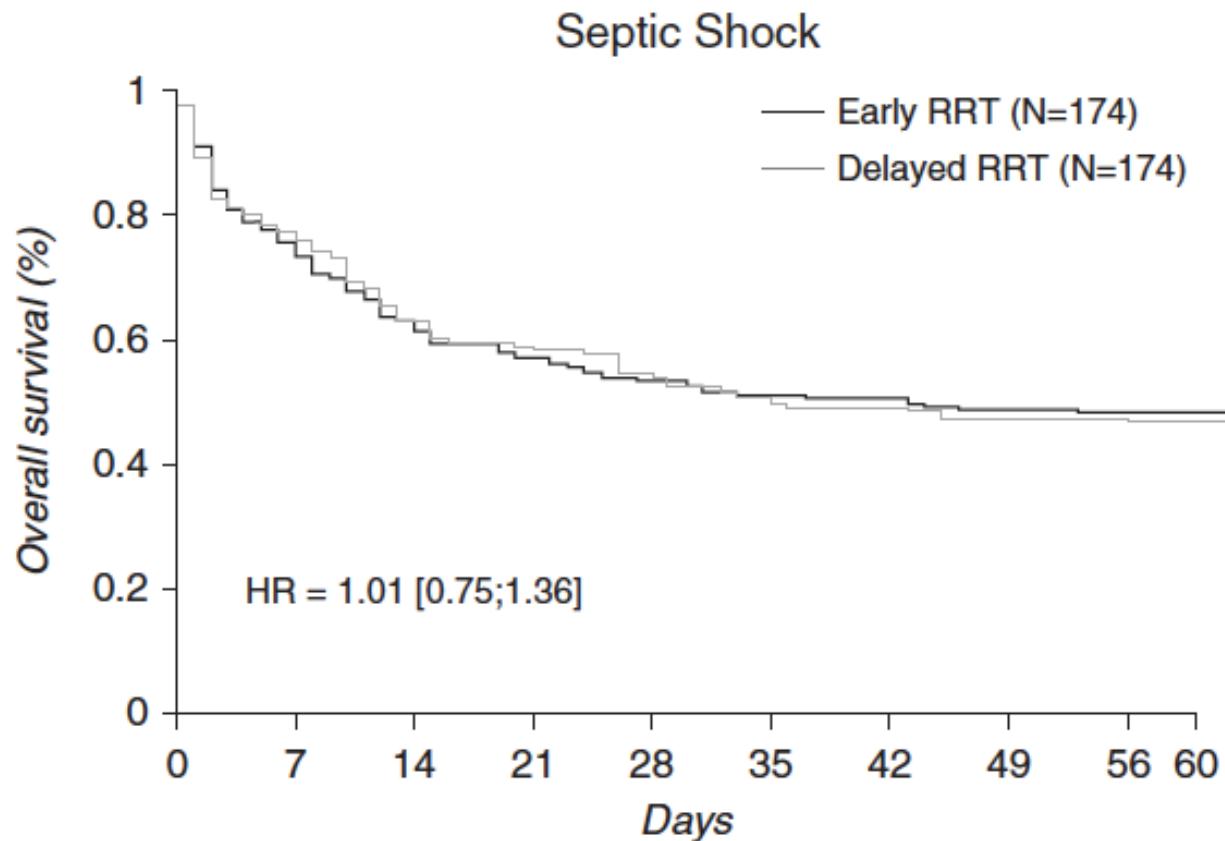
Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

2018

A Post Hoc Analysis of the AKIKI Randomized Clinical Trial

Stéphane Gaudry^{1,2}, David Hajage^{3,4,5}, Frédérique Schortgen⁶, Laurent Martin-Lefevre⁷, Charles Verney¹, Bertrand Pons^{8,9}, Eric Boulet¹⁰, Alexandre Boyer¹¹, Guillaume Chevrel¹², Nicolas Lerolle¹³, Dorothée Carpentier¹⁴,

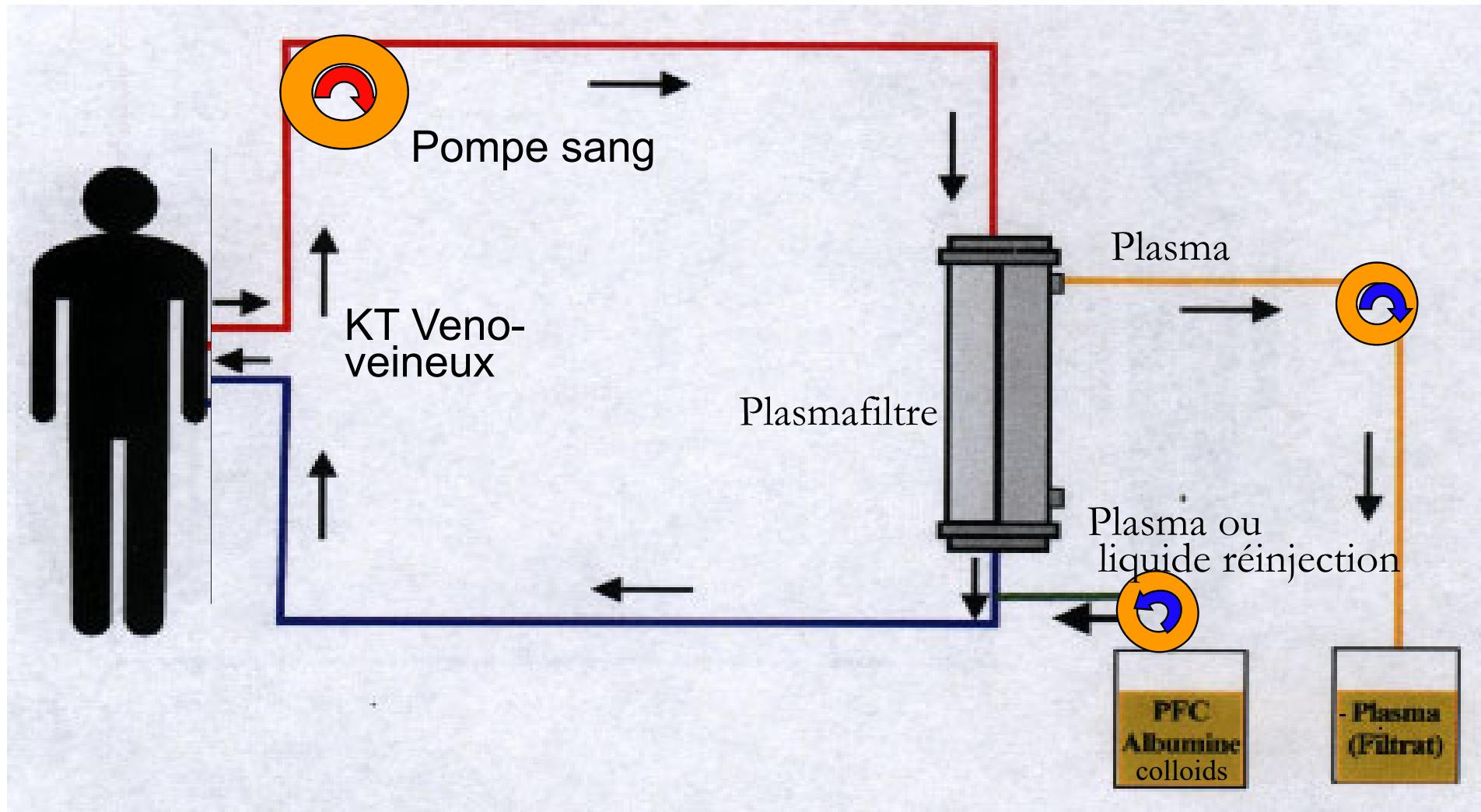
A



Plasmafiltration ?



Plasmafiltration

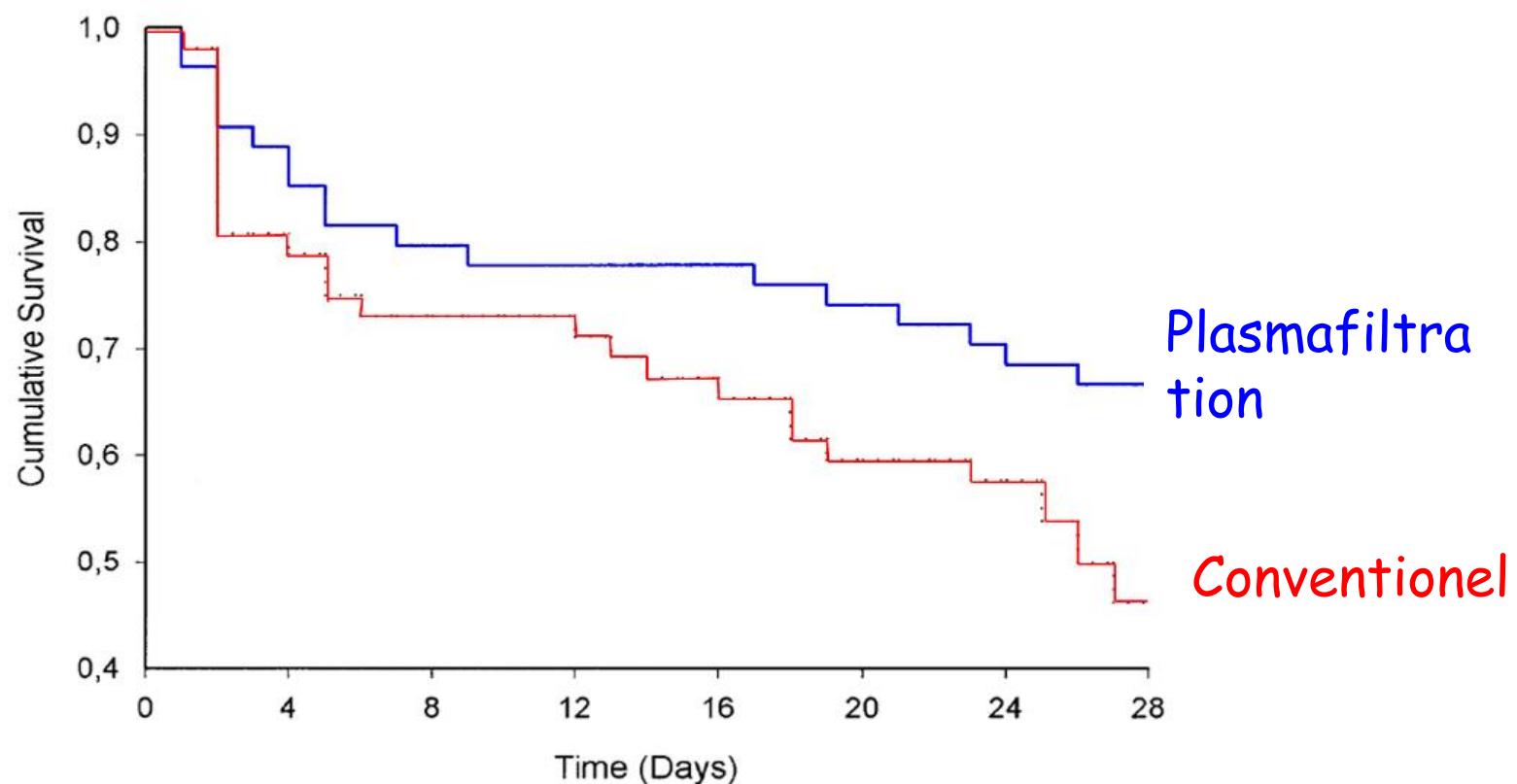




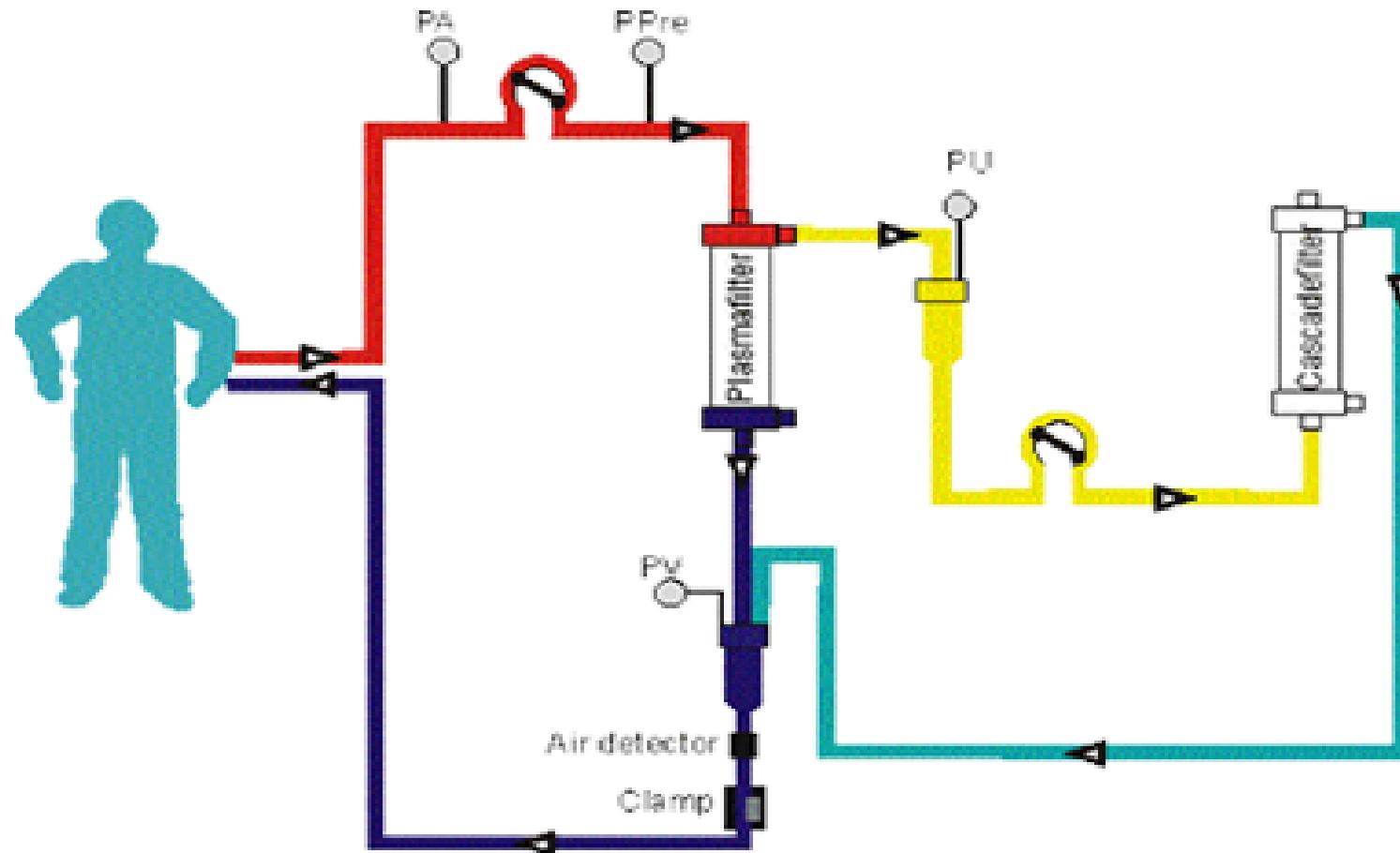
Plasmapheresis in severe sepsis and septic shock: a prospective, randomised, controlled trial

Rolf Busund
Vladimir Koukline
Uri Utrobin
Edvard Nedashkovsky

(2002)



Cascade filtration



Very high volume hemofiltration with the Cascade system in septic shock patients

2015

Jean-Pierre Quenot
 Christine Binquet
 Christophe Vinsonneau
 Saber-David Barbar
 Sandrine Vinault
 Valérie Deckert
 Stéphanie Lemaire
 Ali Ait Hassain
 Rémi Bruyère
 Bertrand Souweine
 Laurent Lagrost
 Christophe Adrie

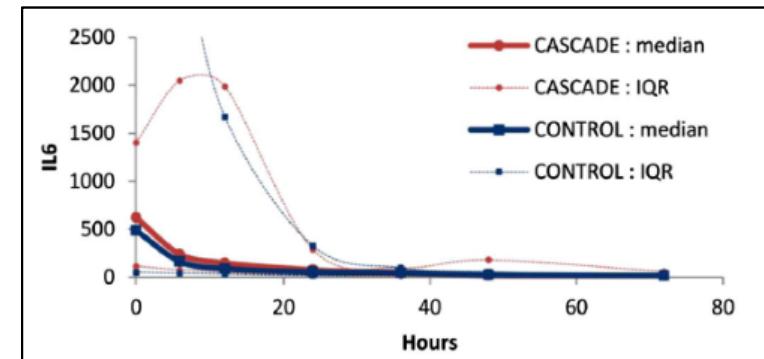
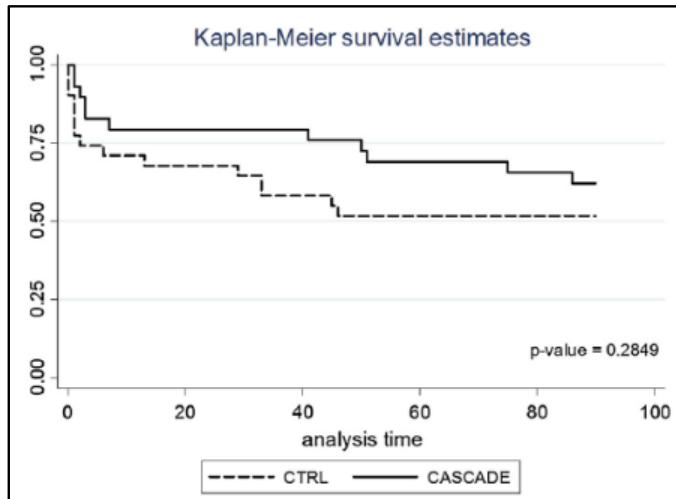


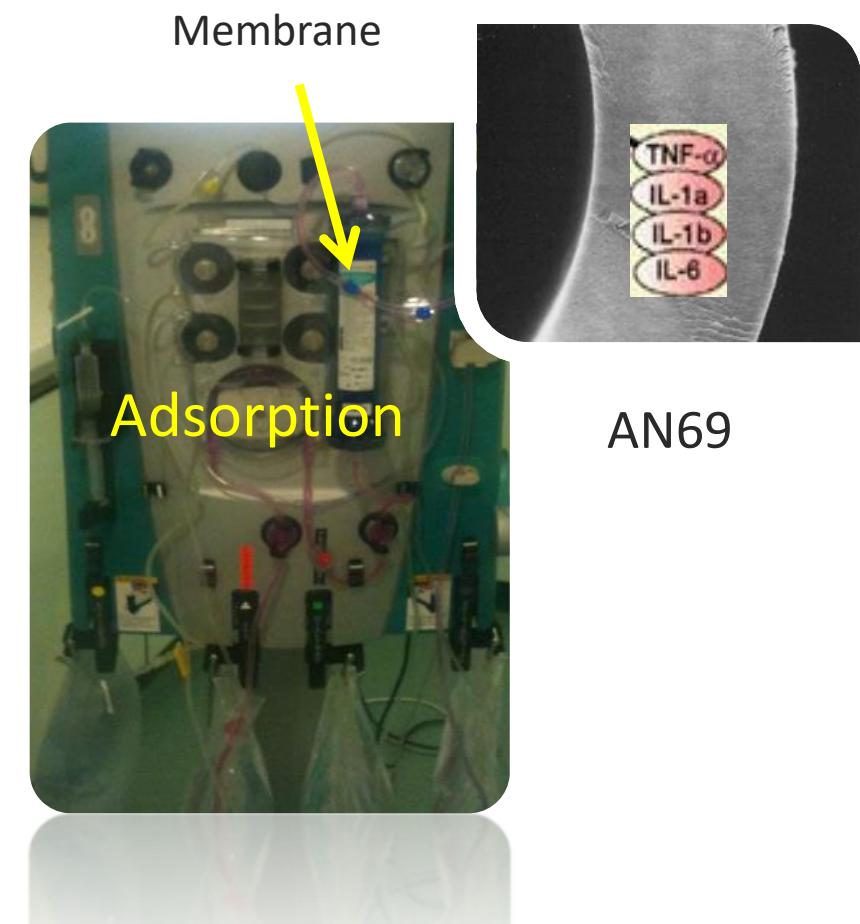
Table 2 Primary and secondary outcomes in the control and Cascade groups

	All (n = 60)	Control (n = 31)	Cascade (n = 29)	p value
Catecholamine-free days up to 28 days	28 [2–25]	22 [11–23]	20 [0–25]	0.78
Mechanical ventilation-free days up to 90 days	70 [0–85]	72 [0–85]	68 [16–83]	0.66
RRT-free days up to 90 days	84 [1–90]	74 [0–90]	85 [46–90]	0.42
ICU-free days up to 90 days	69 [0–83]	70 [0–82]	69 [0–83]	0.92
Death rate				
7 days	15 (25.0)	9 (29.0)	6 (20.7)	0.456
28 days	16 (26.7)	10 (32.3)	6 (20.7)	0.311
90 days	26 (43.3)	15 (48.4)	11 (37.9)	0.414

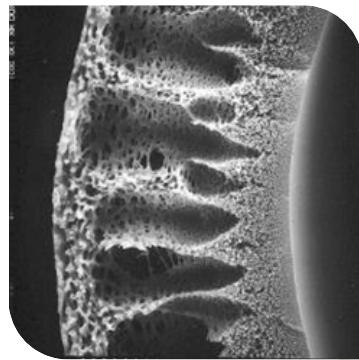
Adsorption



Adsorption ou Absorption ?



Adsorption



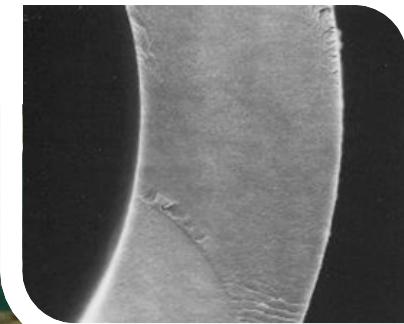
PES



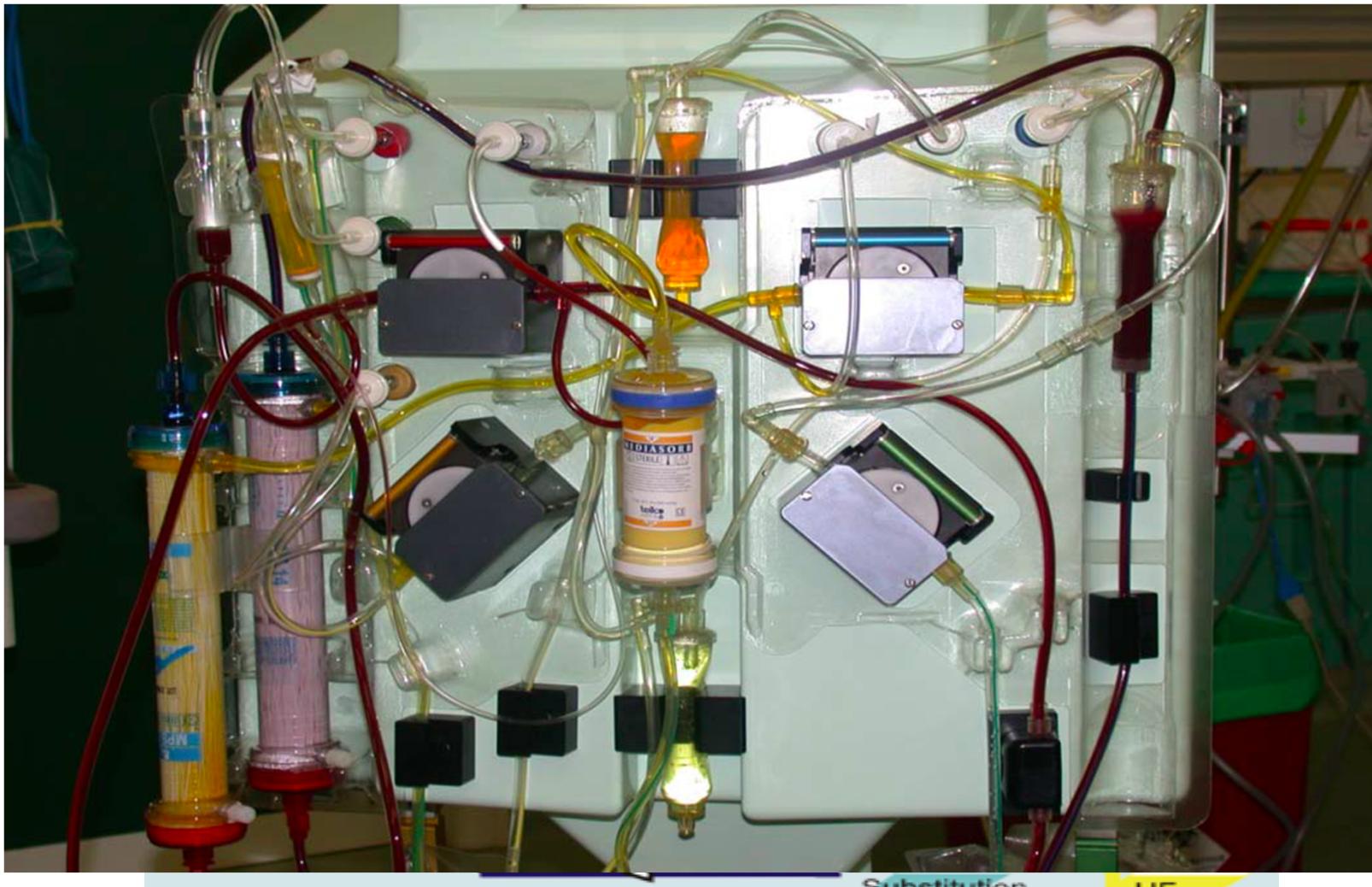
Membrane



AN69



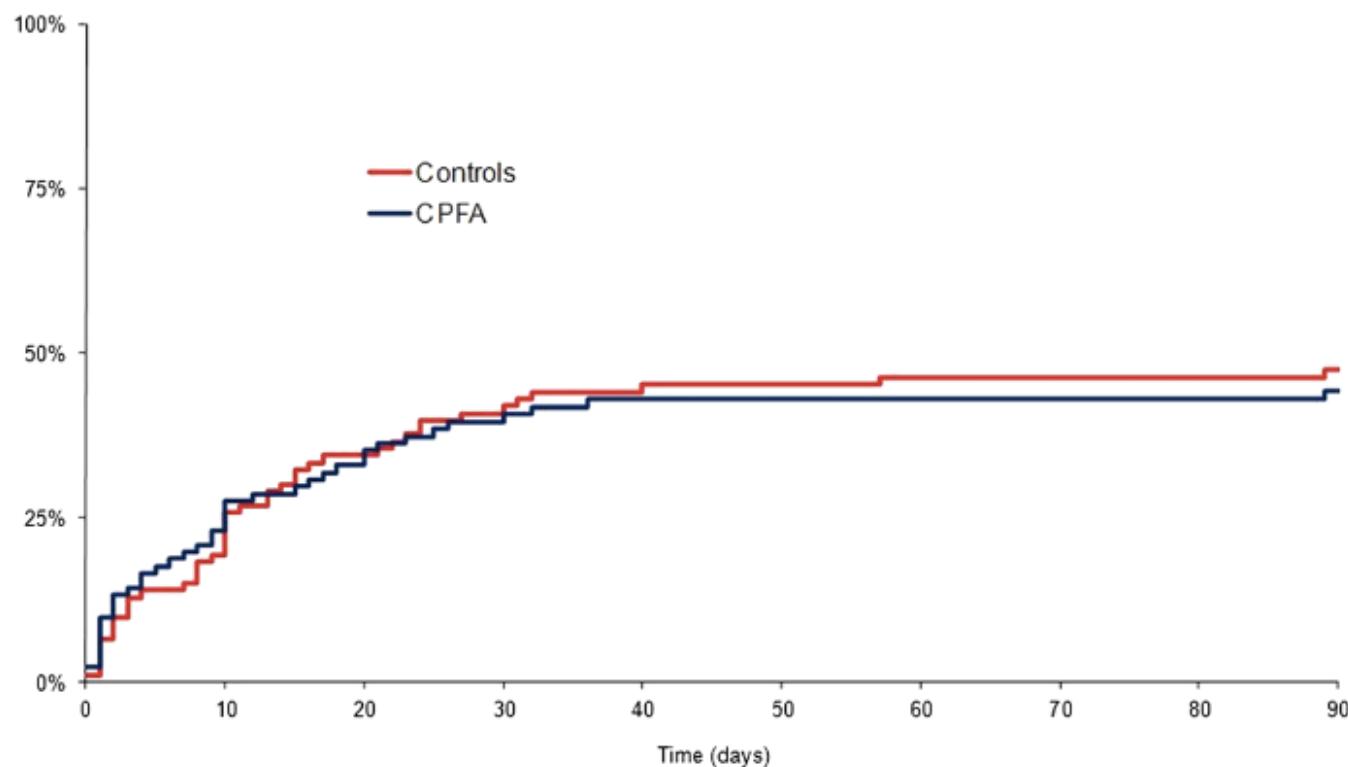
CPFA



Efficacy of coupled plasma filtration adsorption (CPFA) in patients with septic shock: A multicenter randomised controlled clinical trial

2014

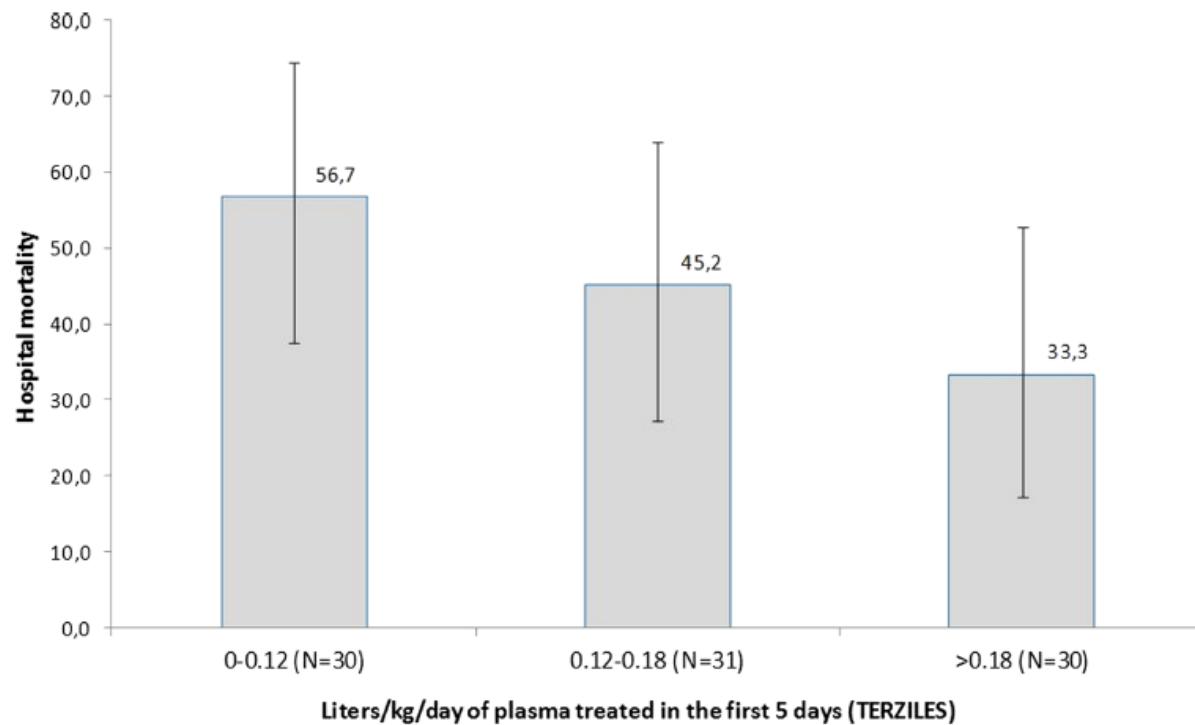
Sergio Livigni,¹ Guido Bertolini,² Carlotta Rossi,² Fiorenza Ferrari,
Michele Giardino,² Marco Pozzato,³ Giuseppe Remuzzi,² GiViTI: (



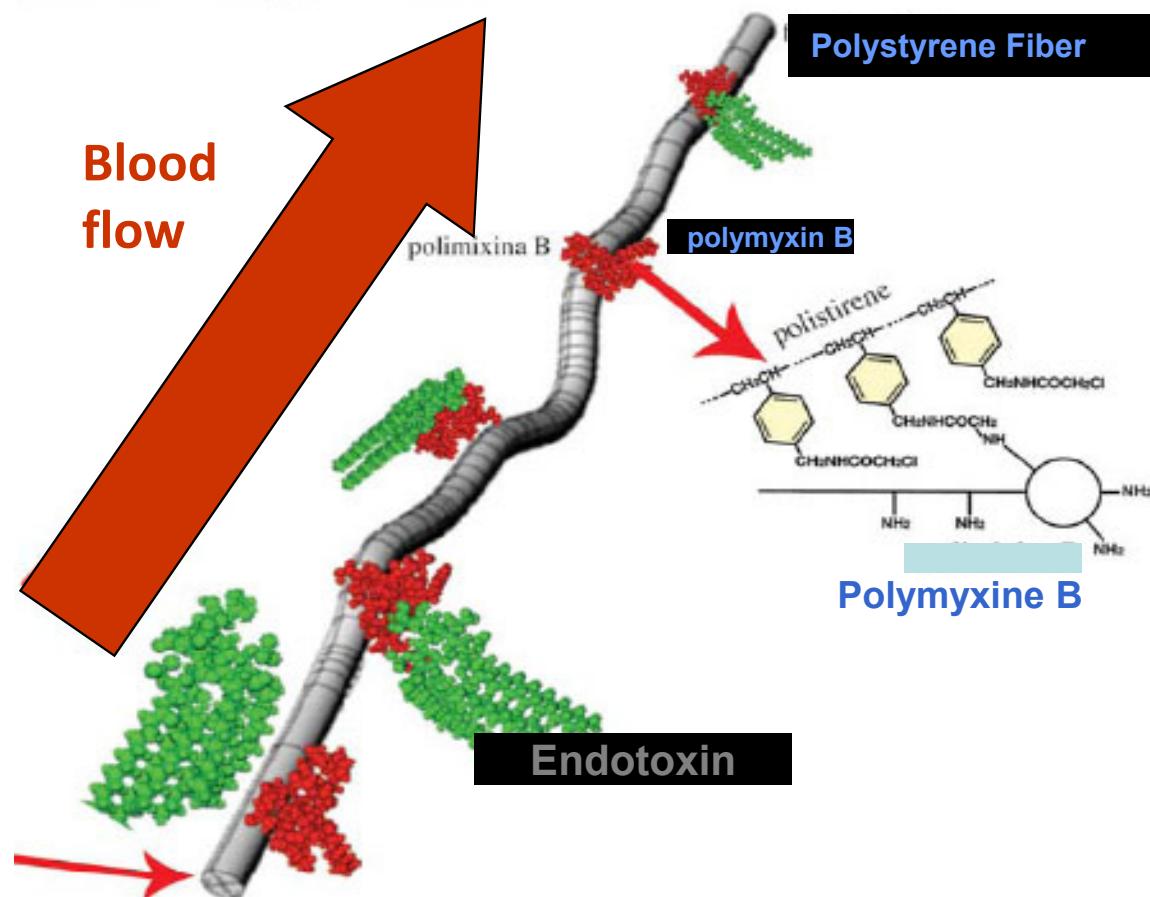
Efficacy of coupled plasma filtration adsorption (CPFA) in patients with septic shock: A multicenter randomised controlled clinical trial

2014

Sergio Livigni,¹ Guido Bertolini,² Carlotta Rossi,² Fiorenza Ferrari,
Michele Giardino,² Marco Pozzato,³ Giuseppe Remuzzi,² GiViTI: (



Polymyxin B membrane



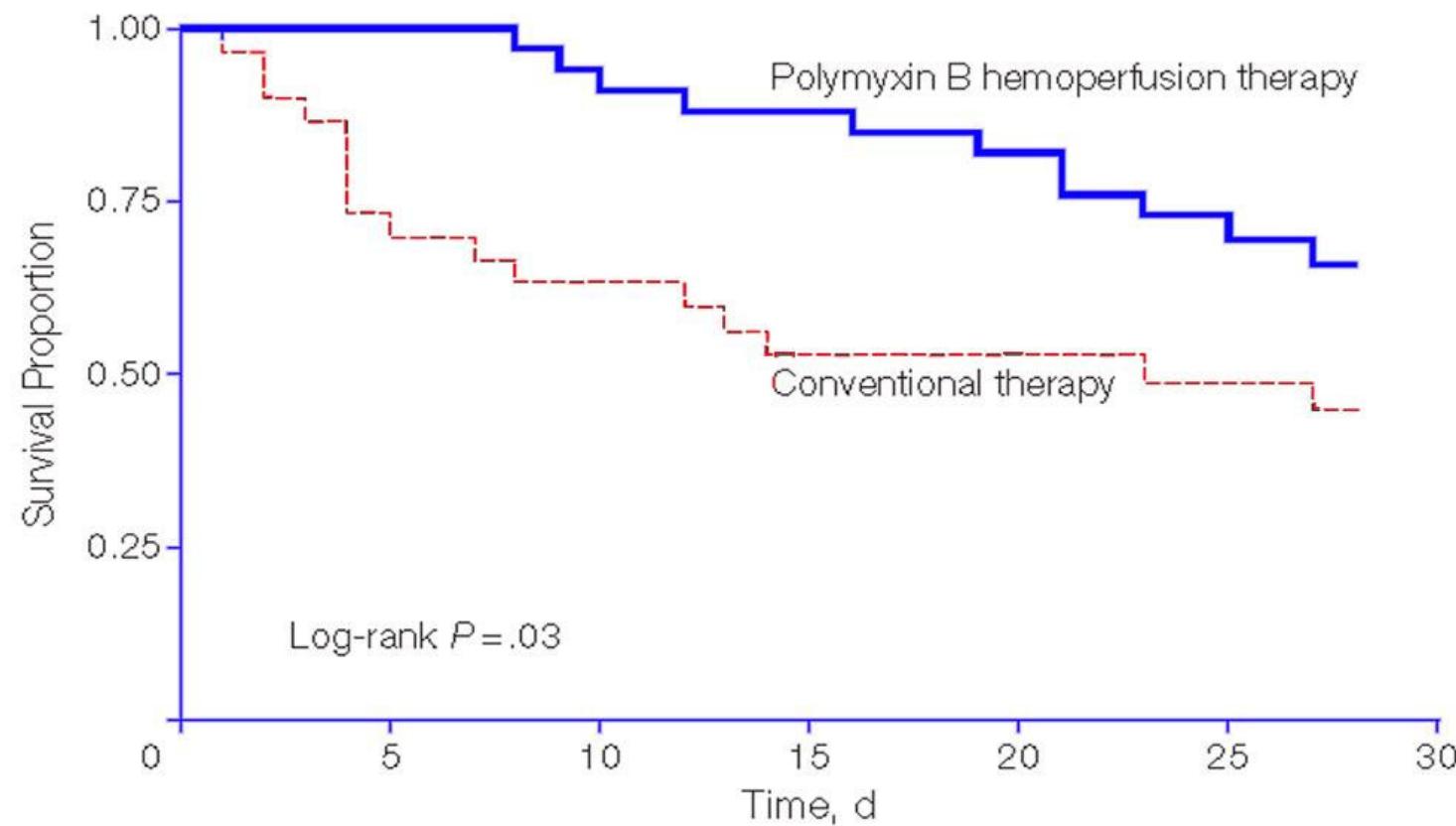


Early Use of Polymyxin B Hemoperfusion in Abdominal Septic Shock

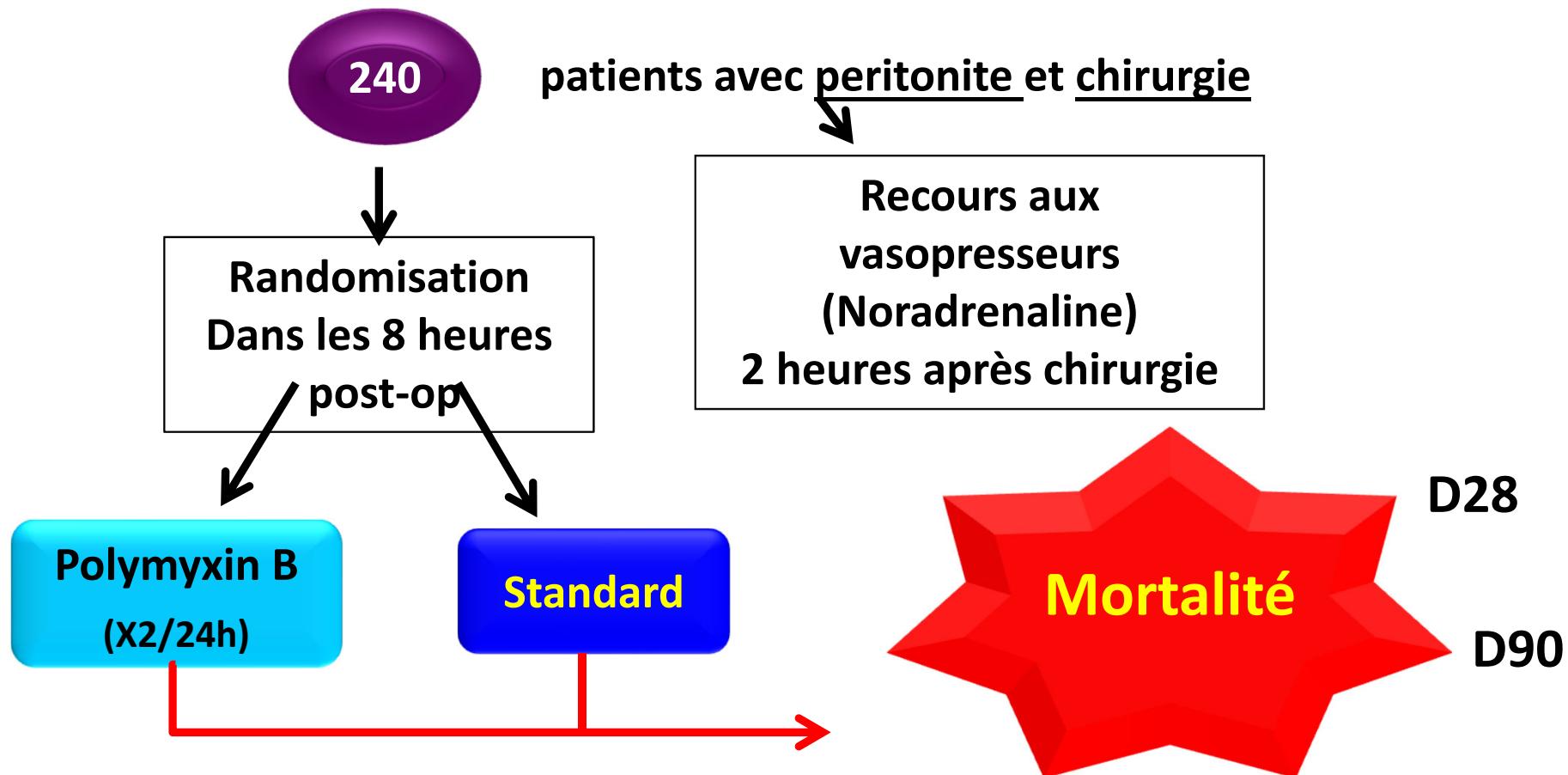
The EUPHAS Randomized Controlled Trial

Dinna N. Cruz, MD, MPH
Massimo Antonelli, MD
Roberto Fumagalli, MD
Francesca Foltran, MD
Nicola Brienza, MD, PhD
Abele Donati, MD

2009



« ABDO-MIX study »

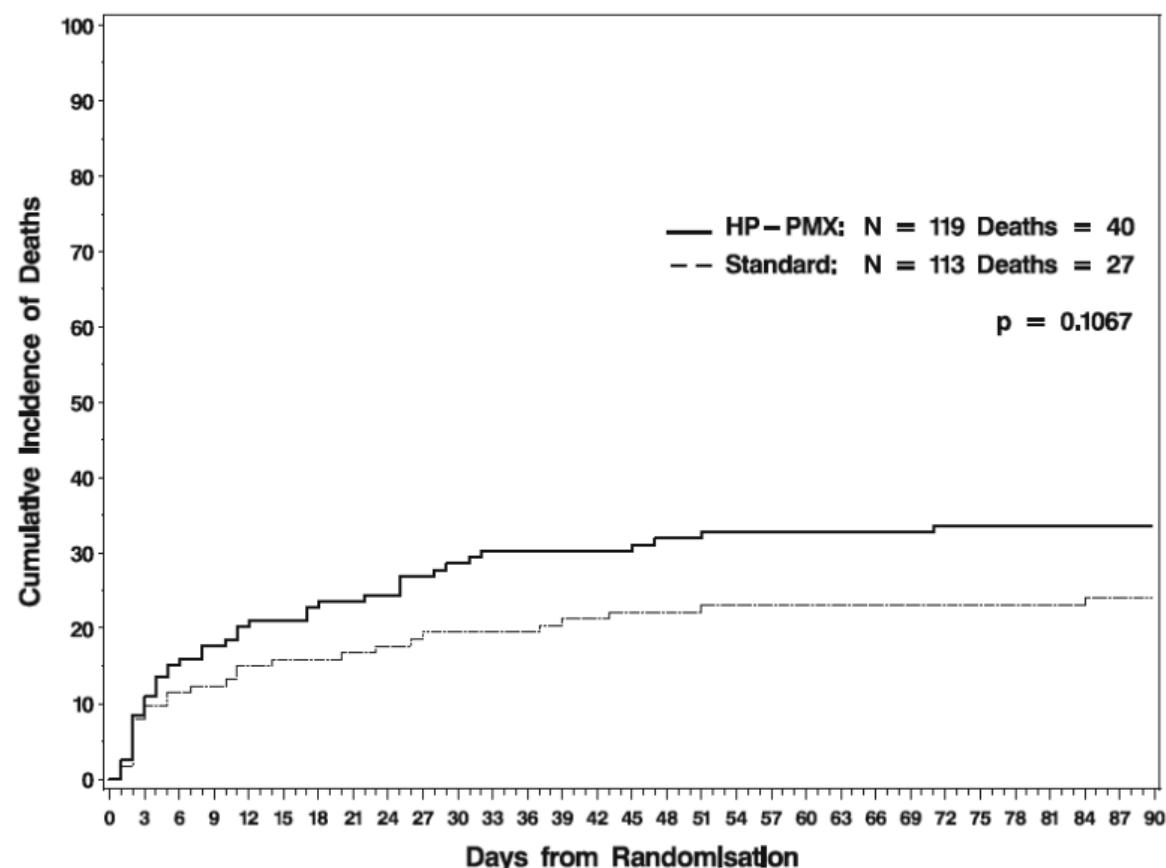




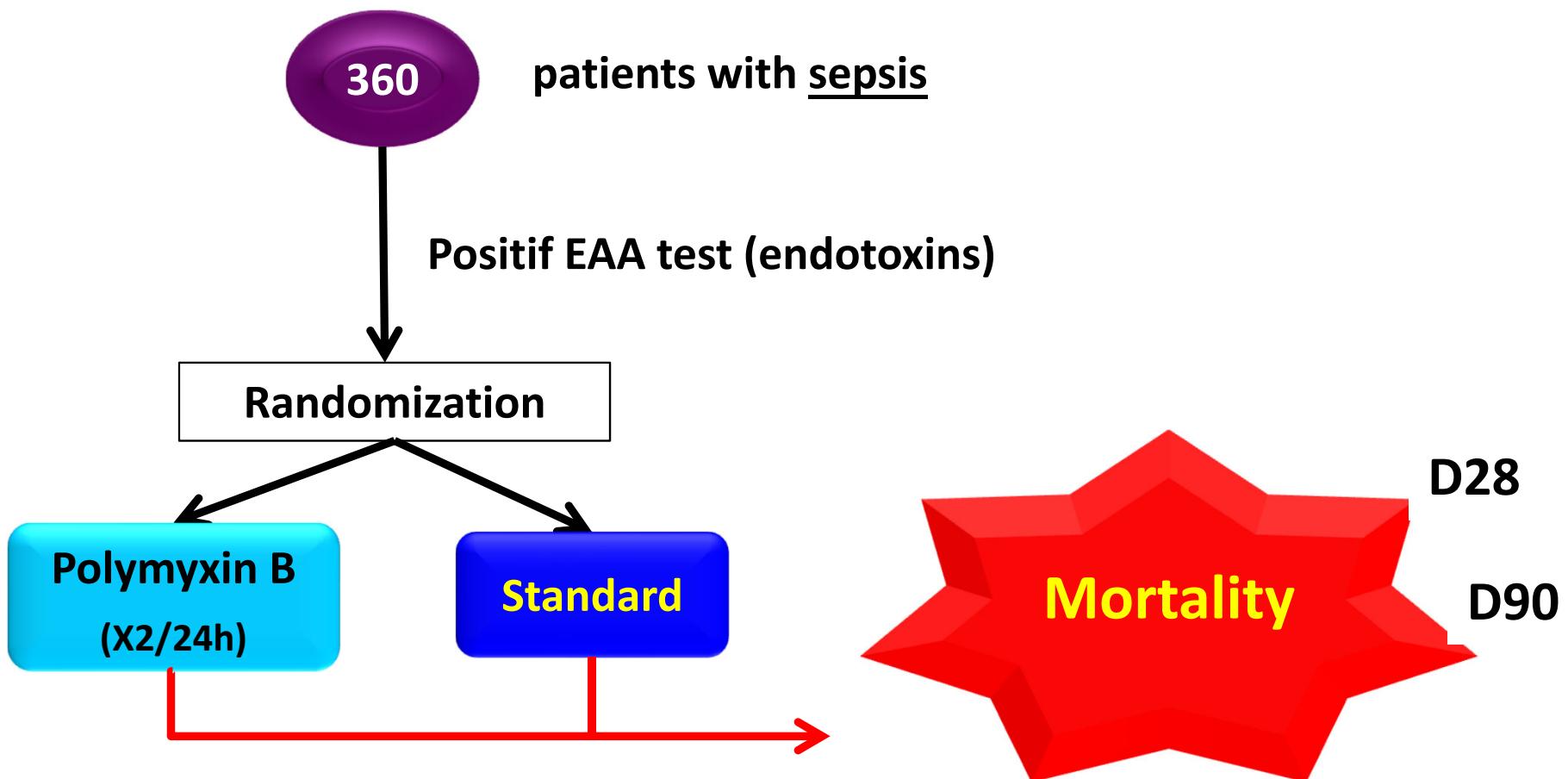
Early use of polymyxin B hemoperfusion in patients with septic shock due to peritonitis: a multicenter randomized control trial

Didier M. Payen
Joelle Guilhot
Yoann Launey
Anne Claire Lukaszewicz
Mahmoud Kaaki
Benoit Veber
Julien Pottecher
Olivier Joannes-Boyau
Laurent Martin-Lefevre

2015



« EUPHRATES study »





Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level

The EUPHRATES Randomized Clinical Trial

R. Phillip Dellinger, MD, MSc; Sean M. Bagshaw, MD, MSc; Massimo Antonelli, MD; Debra M. Foster, BSc; David J. Klein, MD, MBA; John C. Marshall, MD; Paul M. Palevsky, MD; Lawrence S. Weisberg, MD; Christa A. Schorr, DNP, MSN, RN; Stephen Trzeciak, MD, MPH; Paul M. Walker, MD, PhD; for the EUPHRATES Trial Investigators

2018

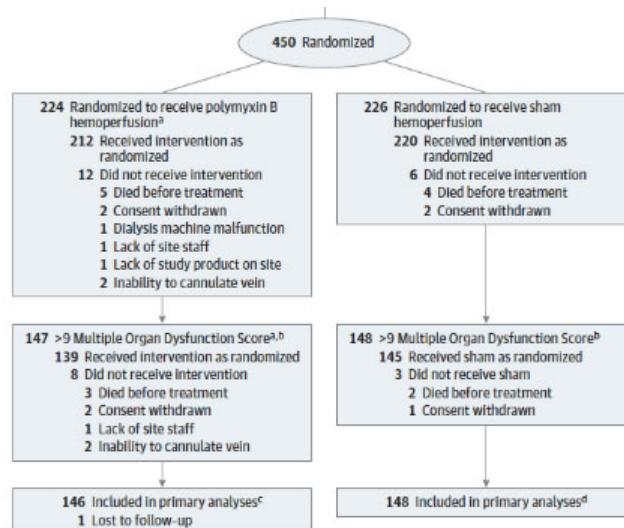
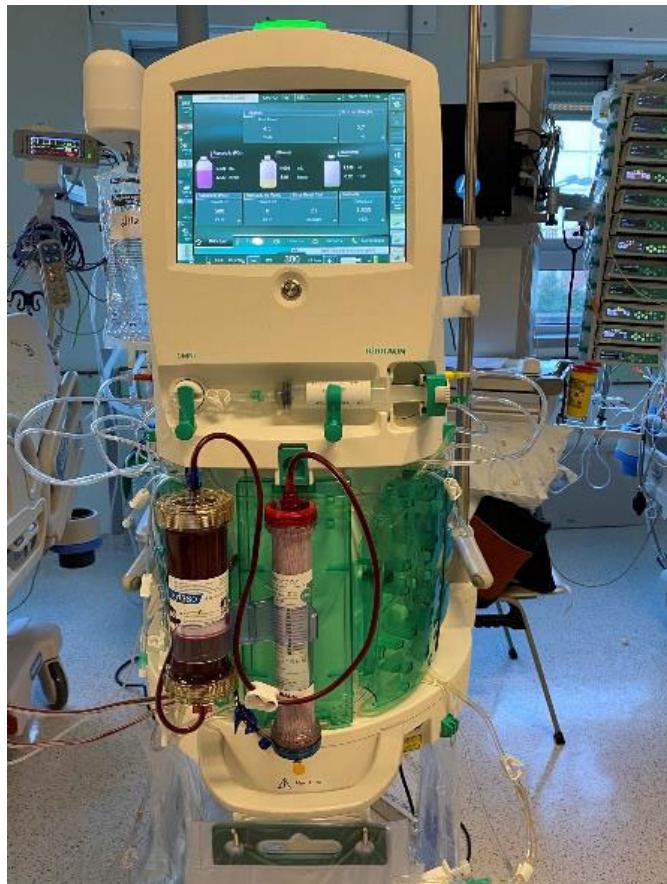


Table 2. Summary of the Primary End Point of 28-Day Mortality for All Participants and for Patients With MODS of More Than 9

	No./Total (%)		(95% CI)		
	Polymyxin-B Hemoperfusion	Sham	Risk Difference	Risk Ratio	P Value ^a
All Participants	84/223 (37.7)	78/226 (34.5)	3.15 (-5.73 to 12.04)	1.09 (0.85 to 1.39)	.49
>9 MODS ^b	65/146 (44.5)	65/148 (43.9)	0.60 (-10.75 to 11.97)	1.01 (0.78 to 1.31)	.92





From AN69 to AN69 Oxiris

Honore PM, Joannes-Boyau et al. ASAIO 2013

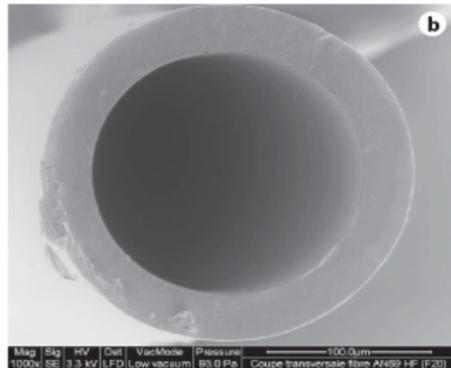
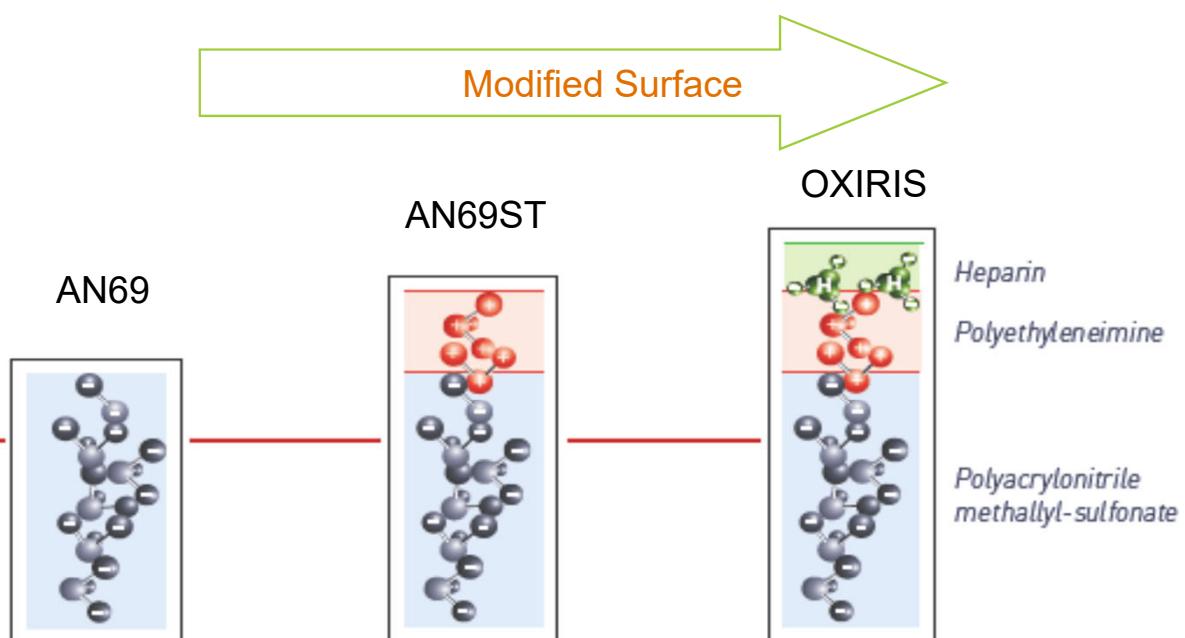
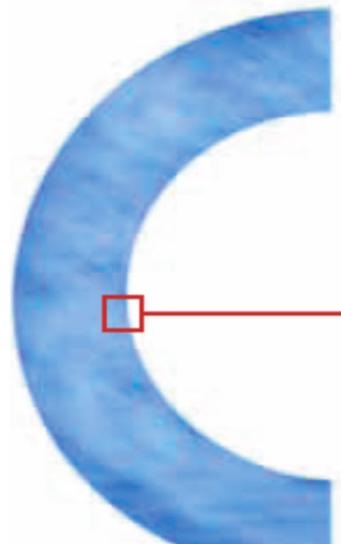
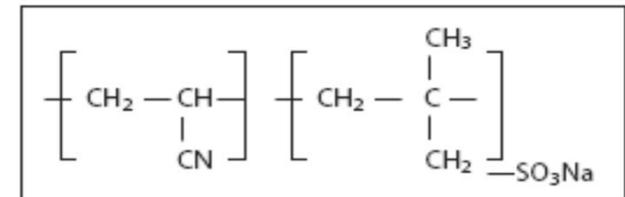
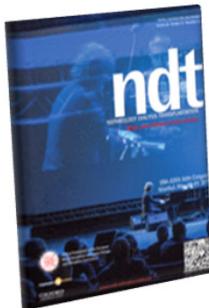


Fig. 1. Chemical formula for AN69 copolymer, consisting of acrylonitrile and sodium methallylsulfonate.





High-volume haemofiltration with a new haemofiltration membrane having enhanced adsorption properties in septic pigs

Thomas Rimmelé^{1,2,3}, Abdulkassar Assadi², Mathilde Catteno¹, Olivier Desebbe^{2,3}, Corine Lambert⁴, Emmanuel Boselli^{1,3}, Joëlle Goudable^{3,5}, Jérôme Étienne^{3,6}, Dominique Chassard^{1,3}, Giampiero Bricca^{2,3} and Bernard Allaouchiche^{1,2,3}

: (2009)

Table 3. Mean \pm SD haemodynamic and biochemical parameters after a 6-h HVHF session, at T6

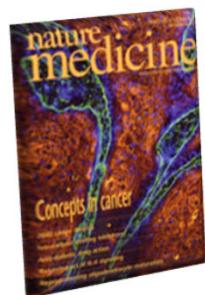
	AN69 mb ($n = 10$)	Treated mb ($n = 10$)	P-value
HR (beats/min)	138 \pm 20	148 \pm 16	0.23
MAP (mmHg)	64 \pm 6	59 \pm 8	0.13
SPAP (mmHg)	39 \pm 9	30 \pm 8	0.029
MPAP (mmHg)	34 \pm 8	24 \pm 7	0.008
PCWP (mmHg)	12 \pm 3	11 \pm 4	0.53
CO (l/min)	6.9 \pm 4.8	5.5 \pm 2.8	0.44
SAR (dyn/s/cm ⁵)	672 \pm 205	797 \pm 346	0.34
PAR (dyn/s/cm ⁵)	325 \pm 186	234 \pm 148	0.24
Epinephrine (mg)	3.27 \pm 3.02	2.11 \pm 1.05	0.27
Crystalloids (ml)	7587 \pm 1456	5937 \pm 1588	0.026
Hydroxyethylstarch (ml)	1912 \pm 538	1437 \pm 320	0.027
pH	7.10 \pm 0.07	7.20 \pm 0.11	0.026
Lactate (mmol/l)	14.11 \pm 3.36	9.61 \pm 4.47	0.02

Table 4. Mean \pm SD serum endotoxins levels (EU/ml)

	AN69 mb ($n = 10$)	Treated mb ($n = 10$)
T0	3.98 \pm 3.31	4.26 \pm 7.68
T1	11.07 \pm 10.64	1.91 \pm 1.19 ^a
T6	2.96 \pm 2.75	2.26 \pm 2.39



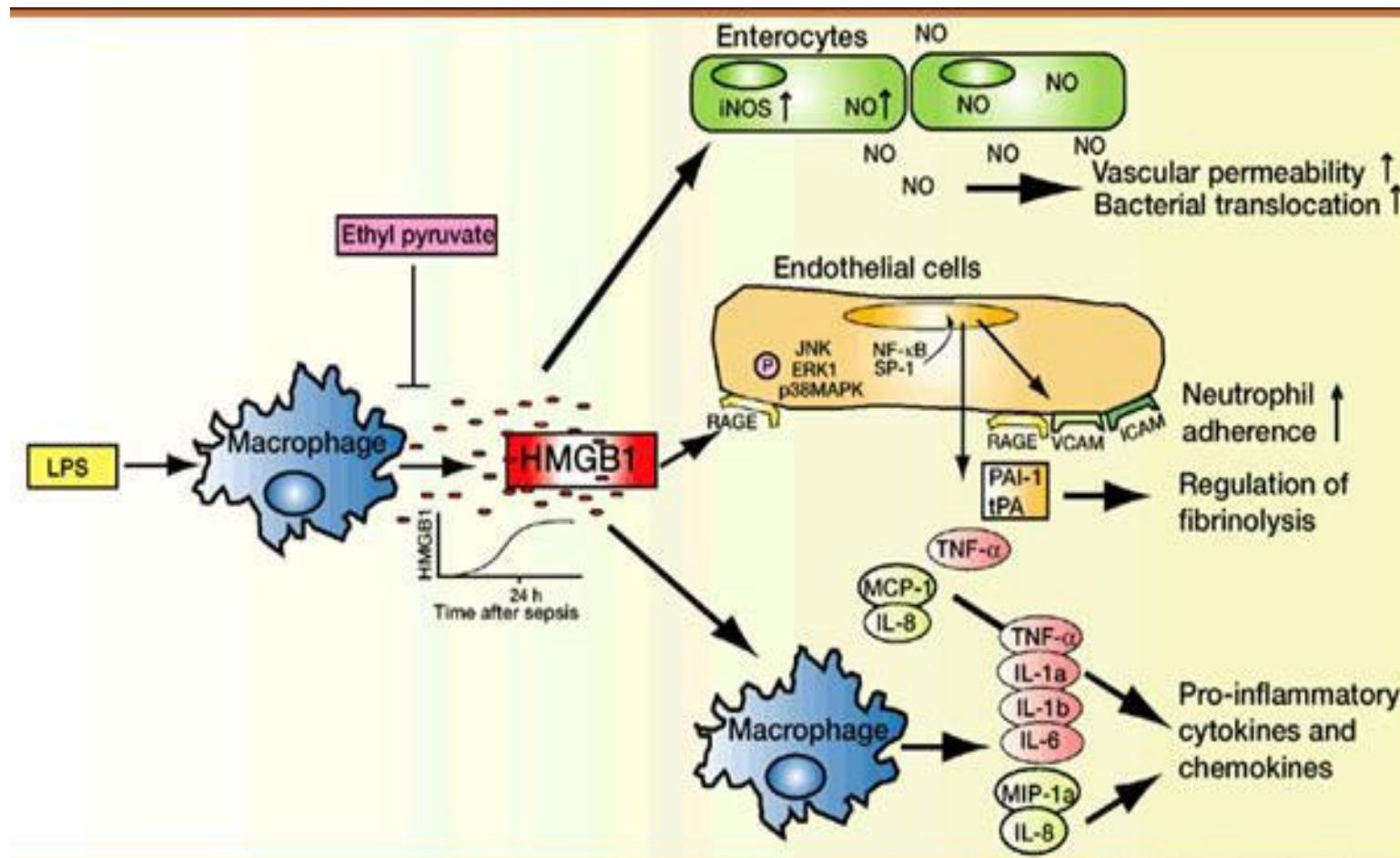
D'après T. Rimmelé

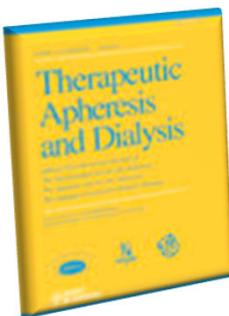


Rationnel pour adsorption : HMGB-1

Riedemann RC

2003





In Vitro Evaluation of High Mobility Group Box 1 Protein Removal with Various Membranes for Continuous Hemofiltration

Miho Yumoto,¹ Osamu Nishida,¹ Kazuhiro Moriyama,¹ Yasuyo Shimomura,¹ Tomoyuki Nakamura,¹ Naohide Kuriyama,¹ Yoshitaka Hara,¹ and Shingo Yamada²

2011

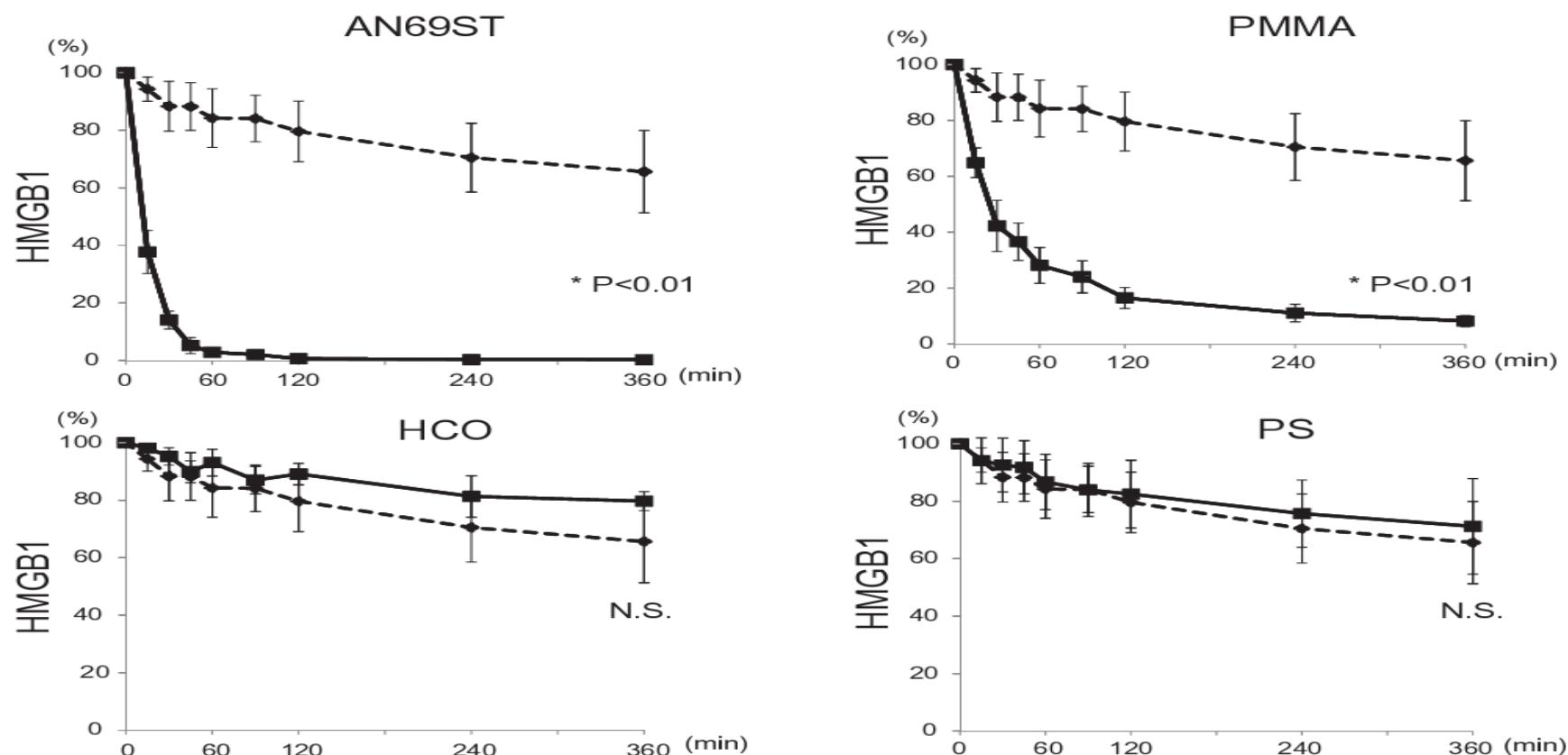


FIG. 4. Time course of high mobility group box 1 protein (HMGB1) levels in the test solution during hemofiltration. Results are shown as mean \pm SD of four experiments. The values at time 0 represent 100%. Dotted line shows the tubing data. These two curves are significantly different from each other ($*P < 0.01$ vs. the tubing). AN69ST, surface-treated polyacrylonitrile; HCO, high cut-off membrane of polyarylethersulfone; PMMA, polymethylmethacrylate; PS, polysulphone.

CONTINUOUS RENAL REPLACEMENT TREATMENT (CRRT) COMBINED WITH ENDOTOXINS REMOVAL IN SEPTIC PATIENTS: A PILOT STUDY

Patrizia Caravetta*, Angela Lappa*, Antonio Menichetti*, Riccardo Barchetta*, Federico Candidi*, Franco Turani*, Mauro Falco*

*San Camillo Forlanini, Rome, Italy; * European Hospital, Rome, Italy

AIM

We tested a recently developed CRRT membrane having enhanced adsorption capability on endotoxins (oXiris™, Gambro Industries, Meyzieu - France). This membrane is a AN 69® based membrane, surface treated with a polyethyleneimmine (PEI) and grafted with heparin (3000 UI/m²) to perform a combined treatment of CRRT and selective adsorption of endotoxins and cytokines in patients with acute kidney injury caused by severe sepsis or septic shock (see Figure 1).



Figure 1 - Structure of oXiris™ membrane.

MATERIALS AND METHODS

We used the oXiris™ membrane in CVVHDF with prescribed effluent dose of 40 ml/kg/h (40% diffusive and 60% convective) with Prismaflex® on 34 patients with AKI having severe sepsis (n=23) or septic shock (n=11) from gram negative (n=28) and positive bacterial (n=6) infection after cardiac surgery. Different anticoagulation strategies (heparin, citrate, no anticoagulation) were applied during the treatments.

RESULTS

34 patients (Age = 65 ± 10 years, Weight = 74 ± 13 Kg, 8 F / 26 M) received CRRT with use of 1.5 ± 0.8 oXiris™ sets per patient for average treatment time of 79 ± 25 hours. Relevant improvements in terms of haemodynamic stability and renal function were found comparing before and after oXiris™ treatment. In particular, an increase of mean arterial pressure and urine output combined with decrease of SOFA scores and norepinephrine dose were found (see Table 1). These results were associated to a relevant decrease of inflammatory markers such as interleukin 6 (IL6) and procalcitonin (PCT) that decrease from 374 ± 501 to 46 ± 57 ($p < 0.01$) pg/ml and from 76 ± 89 to 12 ± 15 ($p < 0.01$) ng/ml respectively. Mortality rate at 28 days of 23% (10/34) and a good renal function recovery (19/23 patients + 1 ESRD) were found.

	PRE TREATMENT	POST TREATMENT	T-TEST STATISTICS
SOFA	12.9 ± 2.6	8.2 ± 3.2	$p < 0.001$
MAP (mmHg)	63 ± 17	80 ± 12	$p < 0.001$
URINE OUTPUT (ml/12h)	540 ± 570	740 ± 660	$p < 0.01$
NOREPINEPHRINE ($\mu\text{g}/\text{kg}/\text{h}$)	0.32 ± 0.32	0.04 ± 0.1	$p < 0.001$

Table 1 - Changes in SOFA, mean arterial pressure (MAP), urine output and norepinephrine dose in patients treated with oXiris™ (mean \pm std).

CONCLUSION

In our experience, the use of this new filter was associated with haemodynamic improvements combined with positive trends of SOFA score and norepinephrine requirements. Moreover, good renal recovery and a survival rate higher than the SOFA predicted one resulted in the population (23% vs 40%). Although this study has many limitations such as lack of endotoxins levels assessment and no randomization analysis, we believe that it will represent a promising result to start further investigations related to the sepsis mediators adsorption combined with AKI treatment by using this newly developed membrane.

P063 - A642 - Continuous renal replacement therapy with the adsorbent membrane oXiris in septic patients: a clinical experience.

F Turani; F Candidi; R Barchetta; E Grilli; A Belli; E Papi; A Di Marzio; M Falco

AURELIA HOSPITAL/EUROPEAN HOSPITAL, Anesthesia Intensive Care, R, Italy

Introduction: Renal failure is an important complication of sepsis and CRRT with adsorbing membranes may be useful in this clinical setting (1). The aims of the study in septic / septic shock patients is to evaluate 1: - the safety of a new hemofilter membrane oXiris with adsorbing properties and anti endotoxin activity 2- the renal and hemodynamic response -3: the changes of endotoxin and pro - inflammatory molecules.

Methods: 40 septic / septic shock patients with renal failure were enrolled in the study. All patients had preoperative endotoxin > 0,6 level , units (EAA Spectral D.) and were submitted to high volume haemodiafiltration (50 ml/kg/h - Prismaflex - Gambro) with a new treated membrane heparin coated (oXiris TM - Gambro). At T0 (pretreatment) T1 (24 hours) the main clinical and biochemical data were evaluated. All data are expressed as mean SD . ANOVA TEST one way with Bonferroni correction was used to evaluate the data changes . P < 0,05 was considered significant

Results: At table 1 are shown the main results of this study.

Conclusions: In septic / septic shock patients with renal failure CRRT with a new treated membrane heparin coated (oXiris TM - Gambro) is clinically feasible , has a positive effect on renal function and hemodynamic. An adsorbing effect on pro - inflammatory mediators may have a role in these results. These data and the trend toward a decrease of endotoxin during the treatment warrant further investigation.

References:

1. Rimmelé T et al. Nephrol Dial Transplant 2009 ; 24 :421-427.

Table 1:

Parameters	Units	T0	T1	p
Creatinine	mg/dl	1,9±1	1,18±1*	p< 0,05
Diuresis	ml/24 /H	1284±78	1573±98	
Norepinephrine	mc/Kg/mn	0,17±2	0,06±1*	p< 0,05
IL6	pg/ml	572±78	278±57*	p< 0,05
Procalcitonine	ng/ml	35±7	15±2*	p< 0,05
Endotoxin	Level/U	0,64±0,2	0,49±0,1	

High cut-off membrane

SEPTEX® et EMIC2®



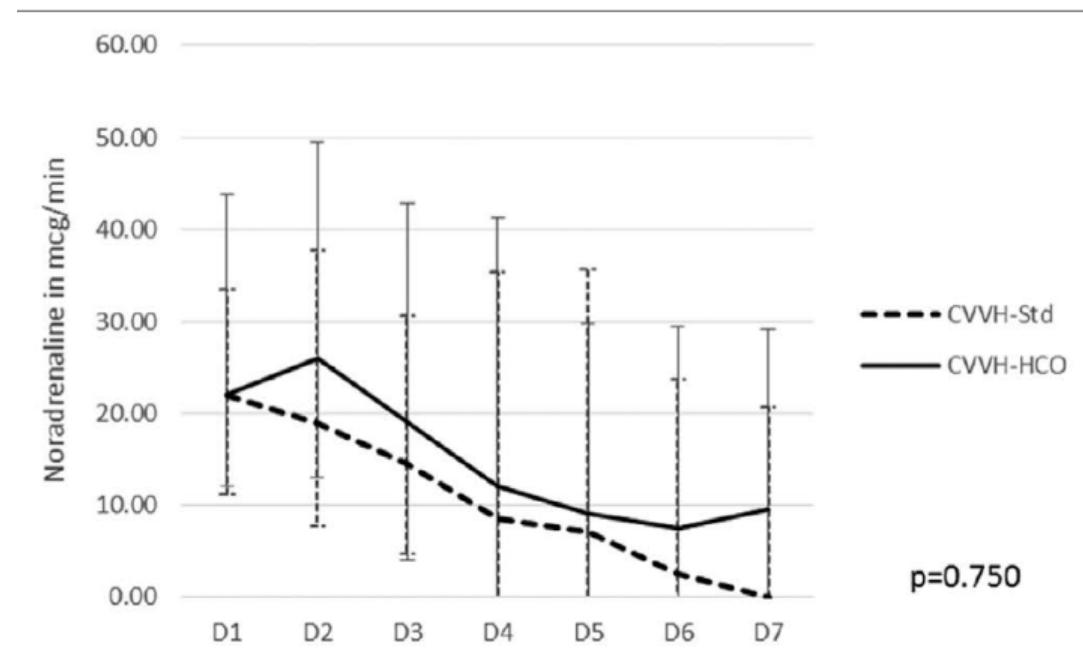
Albumine ?



A Double-Blind Randomized Controlled Trial of High Cutoff Versus Standard Hemofiltration in Critically Ill Patients With Acute Kidney Injury

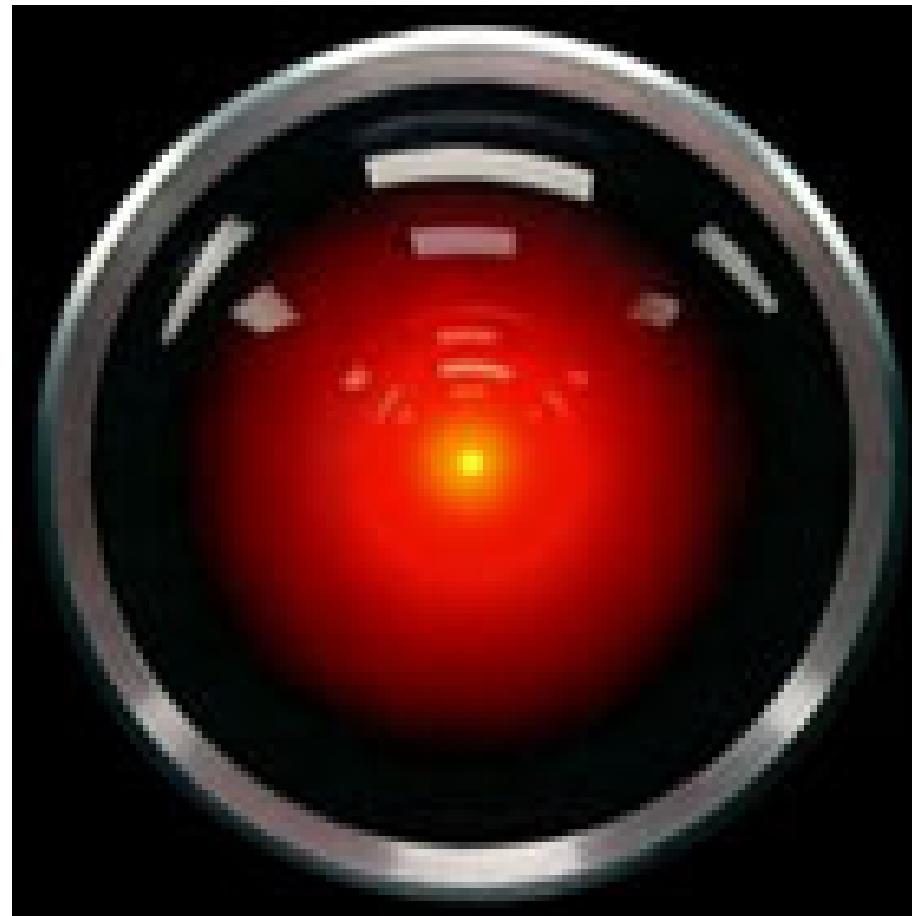
Rafidah Atan, PhD¹; Leah Peck, GradCert(Crit Care)²; John Prowle, MD^{3,4}; Elisa Licari, MD⁵; Glenn M. Eastwood, PhD²; Markus Storr, PhD⁶; Hermann Goehl, MSc⁶; Rinaldo Bellomo, MD^{2,7}

2018



Outcomes	Continuous Venovenous Hemofiltration-High Cutoff, n (%)	Continuous Venovenous Hemofiltration-Standard, n (%)	Unadjusted OR (95% CI)	Adjusted OR ^a (95% CI)
ICU mortality	18 (50)	12 (31.6)	2.17 (0.84–5.58); $p = 0.109$	2.13 (0.69–6.65); $p = 0.191$
Hospital mortality	20 (55.6)	13 (34.2)	2.40 (0.94–6.15); $p = 0.067$	2.49 (0.81–7.66); $p = 0.112$

Futur ?

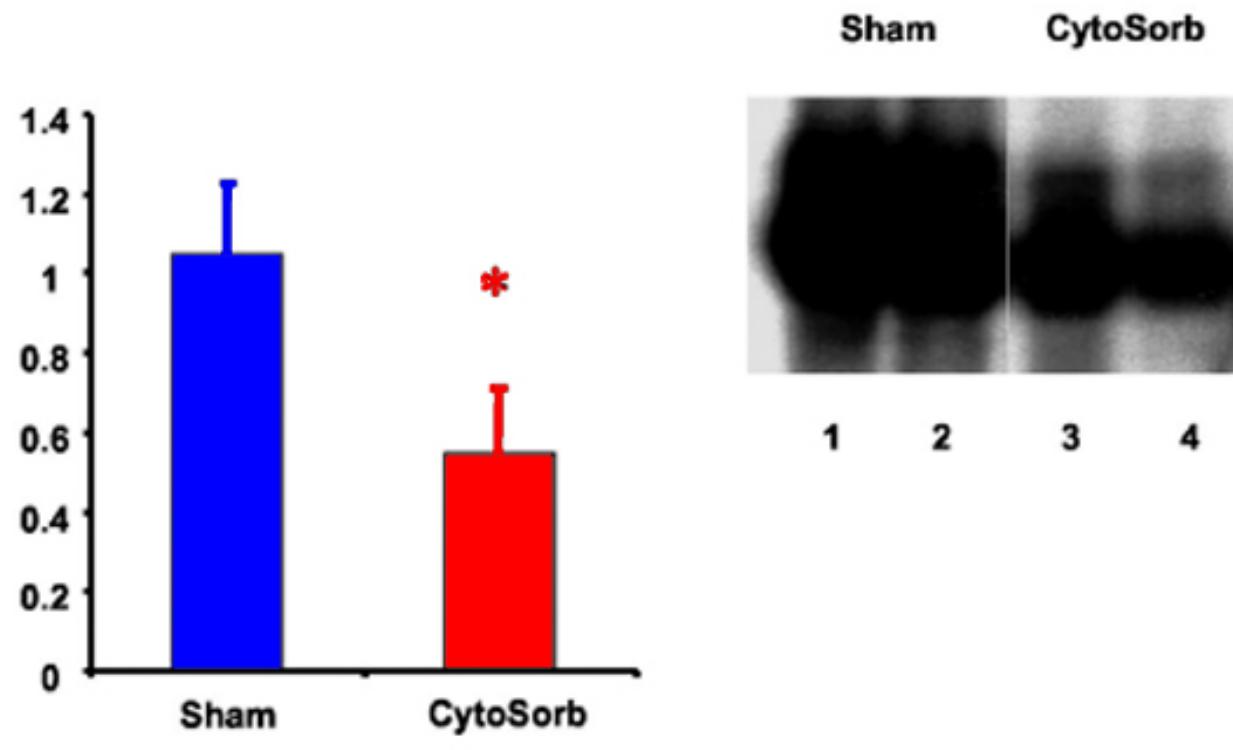




Hemoabsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor- κ B DNA binding, and improves short-term survival in lethal endotoxemia*

John A. Kellum, MD, FCCM; Mingchen Song, MD, PhD; Ramesh Venkataraman, MD

2004



Epuration du NF κ B du tissu hépatique

Blood Purification With CytoSorb in Critically Ill Patients: Single-Center Preliminary Experience

*Maria Grazia Calabò, *Daniela Febres, *Gaia Recca, *Rosalba Lembo,
*Evgeny Fominskiy , *Anna Mara Scandroglio, *†Alberto Zangrillo, and
*†Federico Pappalardo

2018



Values	Peak during treatment	End of treatment	P value
Total bilirubin (mg/dL)	11.6 ± 9.2	6.8 ± 5.1	0.005
Lactate (mmol/L)	12.1 ± 8.7	2.9 ± 2.5	<0.001
CPK (U/L)	2416 (670–8615)	281 (44–2769)	<0.001
LDH (U/L)	1230 (860–3157)	787 (536–1148)	<0.001

Leukocyte capture and modulation of cell-mediated immunity during human sepsis: an *ex vivo* study

Thomas Rimmelé¹, Ata Murat Kaynar¹, Joseph N McLaughlin¹, Jeffery V Bishop¹, Morgan V Fedorchak²,

2013

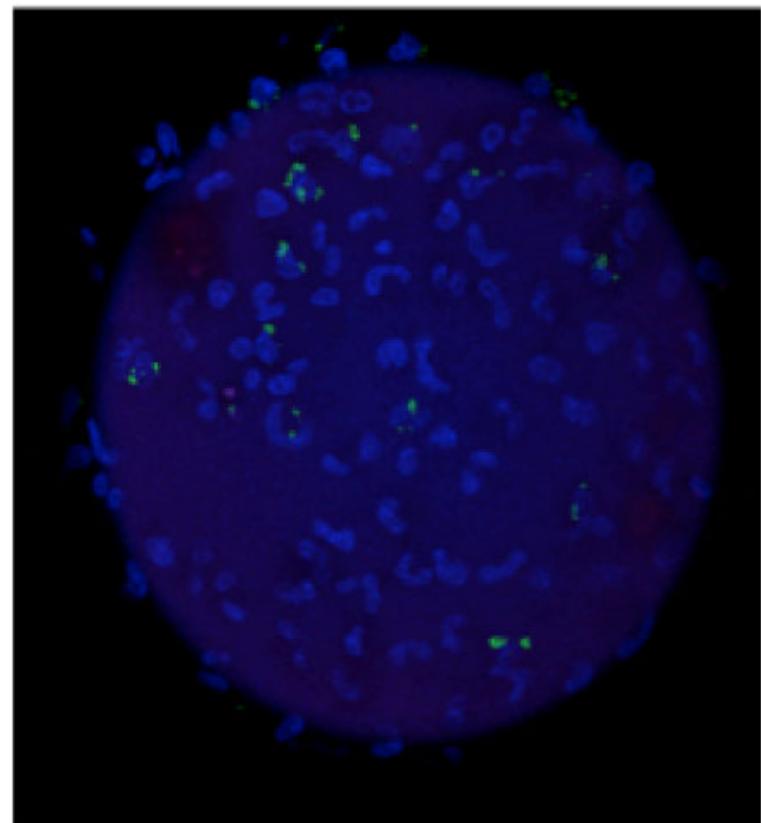
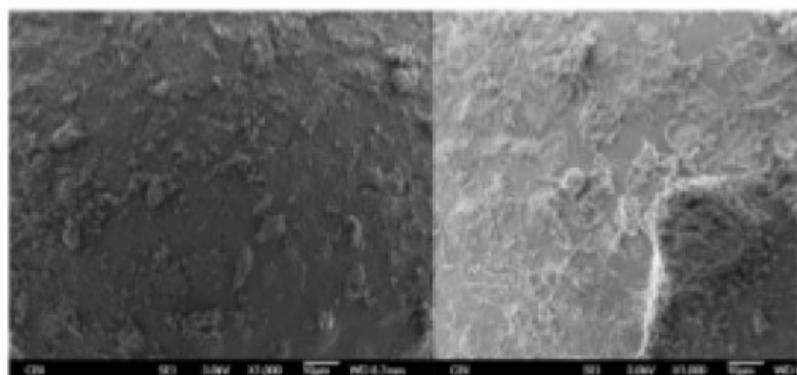
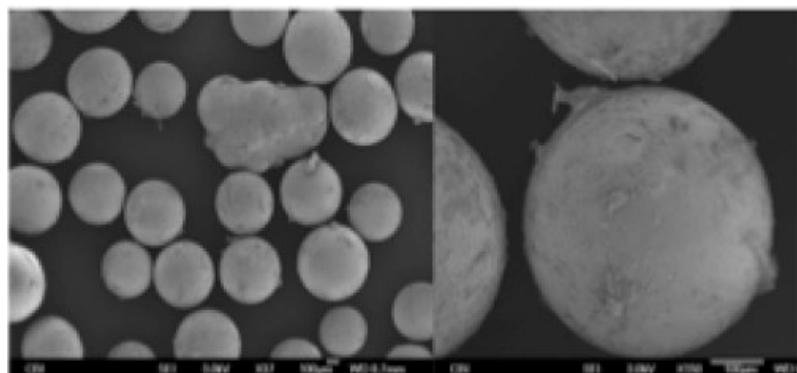


Figure 3 Electron microscopy (EM) and immunofluorescence (IF) images showing cell adsorption onto the beads.

A Biomimetic Membrane Device That Modulates the Excessive Inflammatory Response to Sepsis

Feng Ding¹, Joon Ho Song², Ju Young Jung³, Liandi Lou⁴, Min Wang⁴, Linda Charles⁴, Angela Westover⁴, Peter L. Smith⁴, Christopher J. Pino⁴, Deborah A. Buffington⁴, H. David Humes^{4,5*}

2011

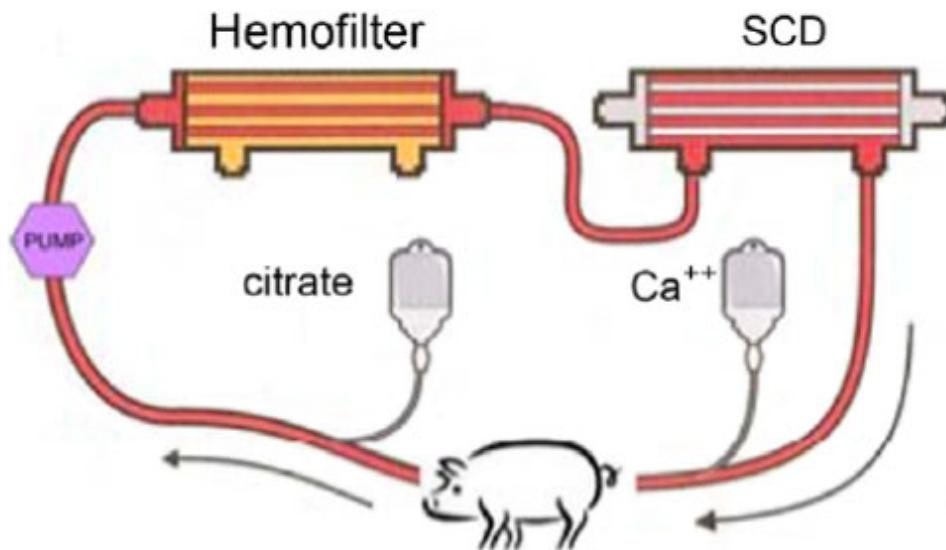
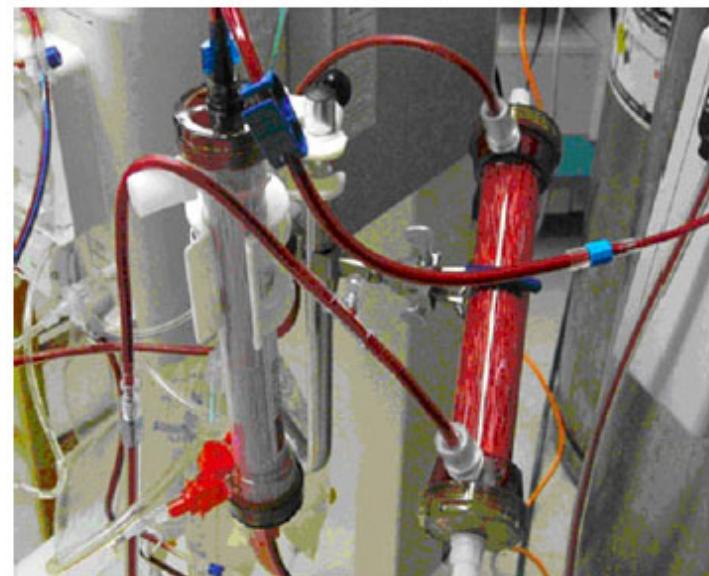


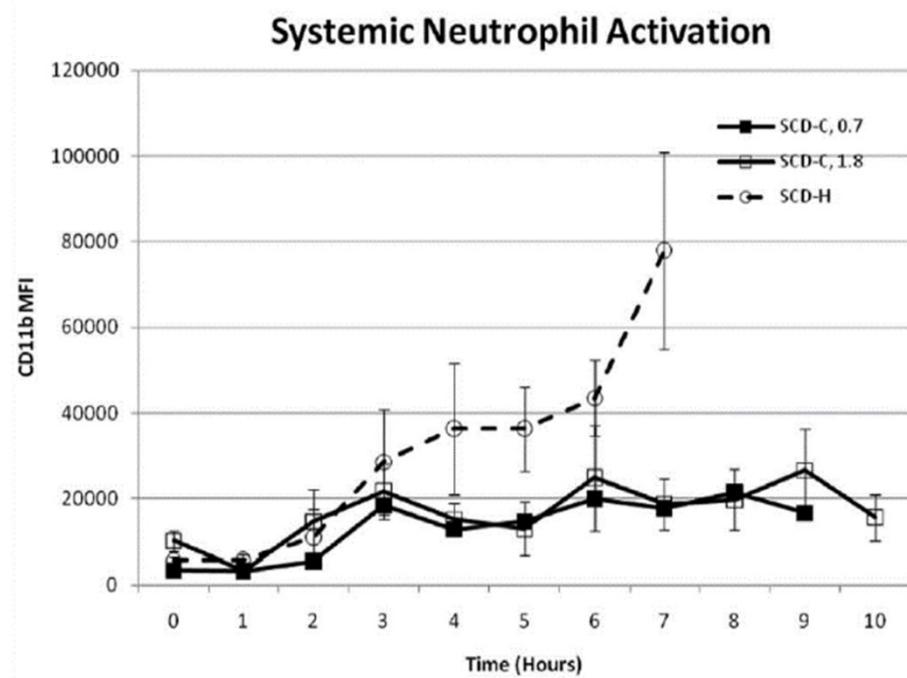
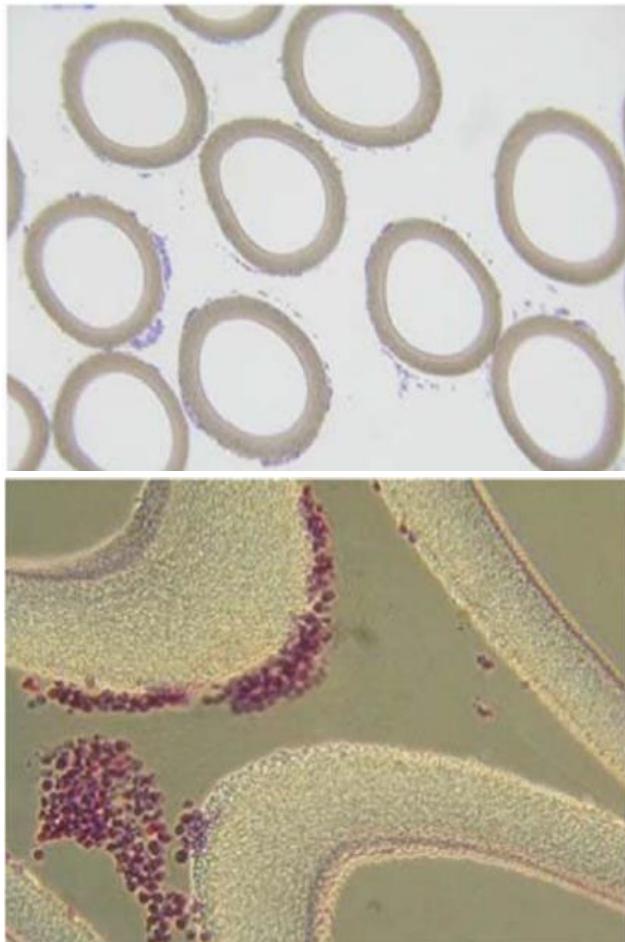
Figure 1. Extracorporeal circuit with SCD.

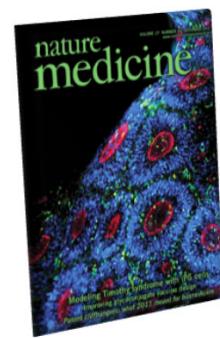


A Biomimetic Membrane Device That Modulates the Excessive Inflammatory Response to Sepsis

Feng Ding¹, Joon Ho Song², Ju Young Jung³, Liandi Lou⁴, Min Wang⁴, Linda Charles⁴, Angela Westover⁴, Peter L. Smith⁴, Christopher J. Pino⁴, Deborah A. Buffington⁴, H. David Humes^{4,5*}

2011

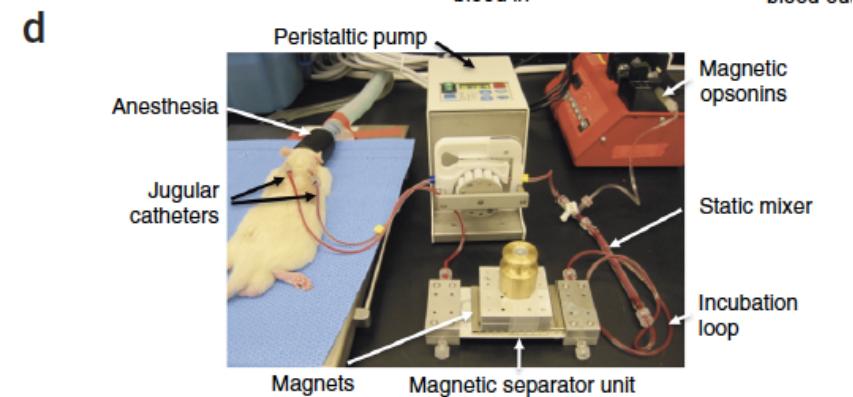
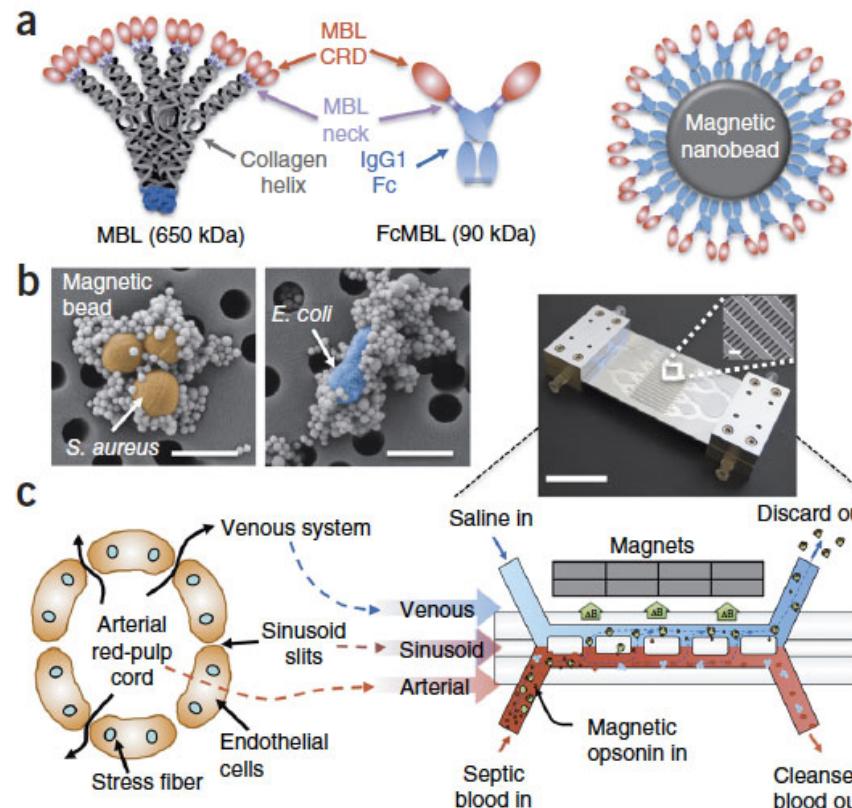




An extracorporeal blood-cleansing device for sepsis therapy

Joo H Kang^{1-3,7}, Michael Super^{1,7}, Chong Wing Yung^{1,2}, Ryan M Cooper^{1,2,4}, Karel Domansky¹, Amanda R Graveline¹, Tadanori Mammoto², Julia B Berthet¹, Heather Tobin², Mark J Cartwright¹,

2014



Conclusion

- Des théories physiopathologiques prometteuses
- Des études animales et humaines encourageantes
- MAIS aucun RCT montrant un réel bénéfice

- Très couteux et techniquement compliqué
- Nouveaux essais attendus et nécessaires

L'utilisation de ces techniques en dehors de la recherche n'est pas recommandée