

Extrakorporale Therapie in der Sepsis

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Extrakorporale Therapie in der Sepsis

1) The unmet medical need

2) More than removal

3) Studies we need

Extrakorporale Therapie in der Sepsis

1) The unmet medical need

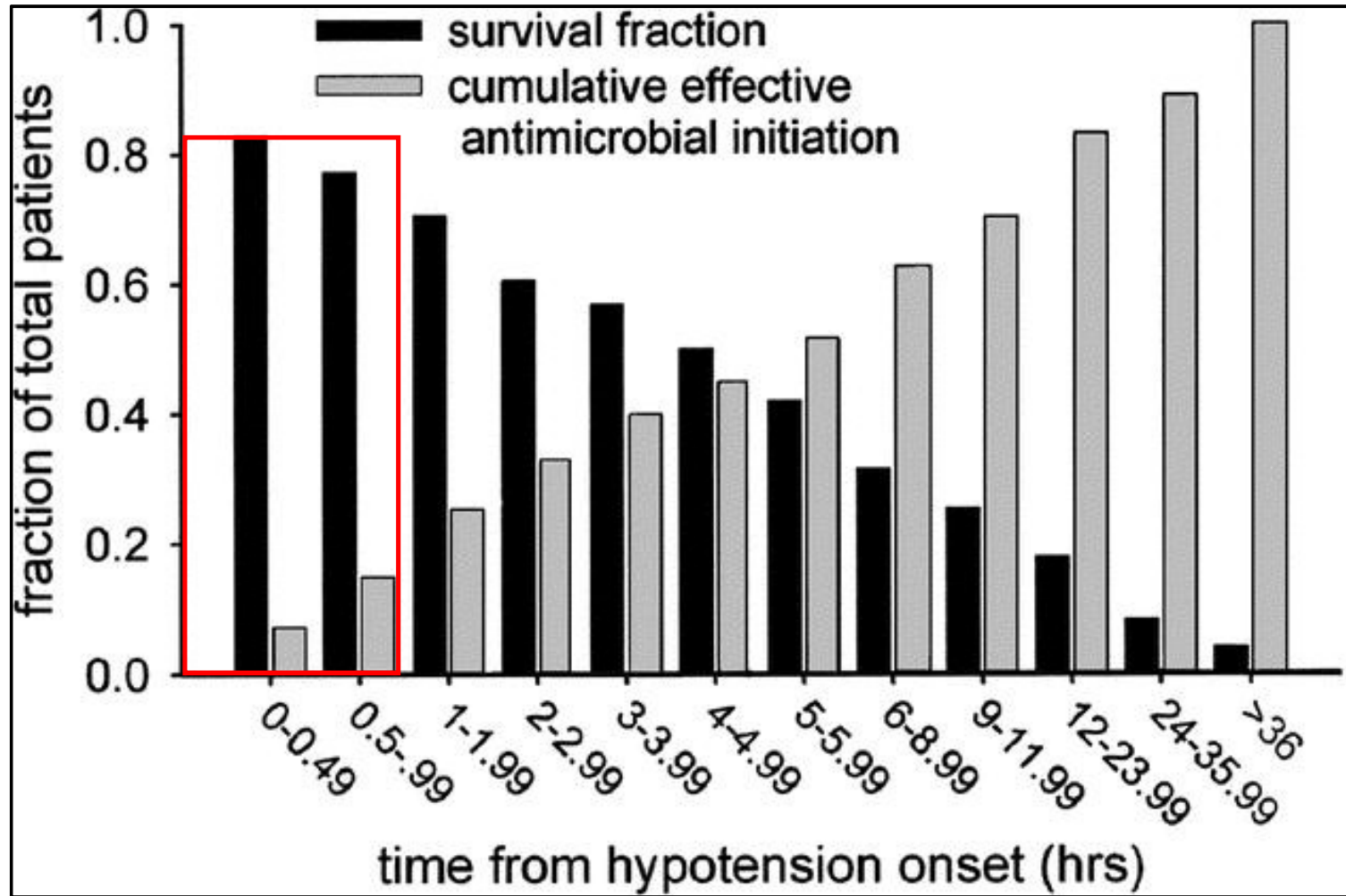
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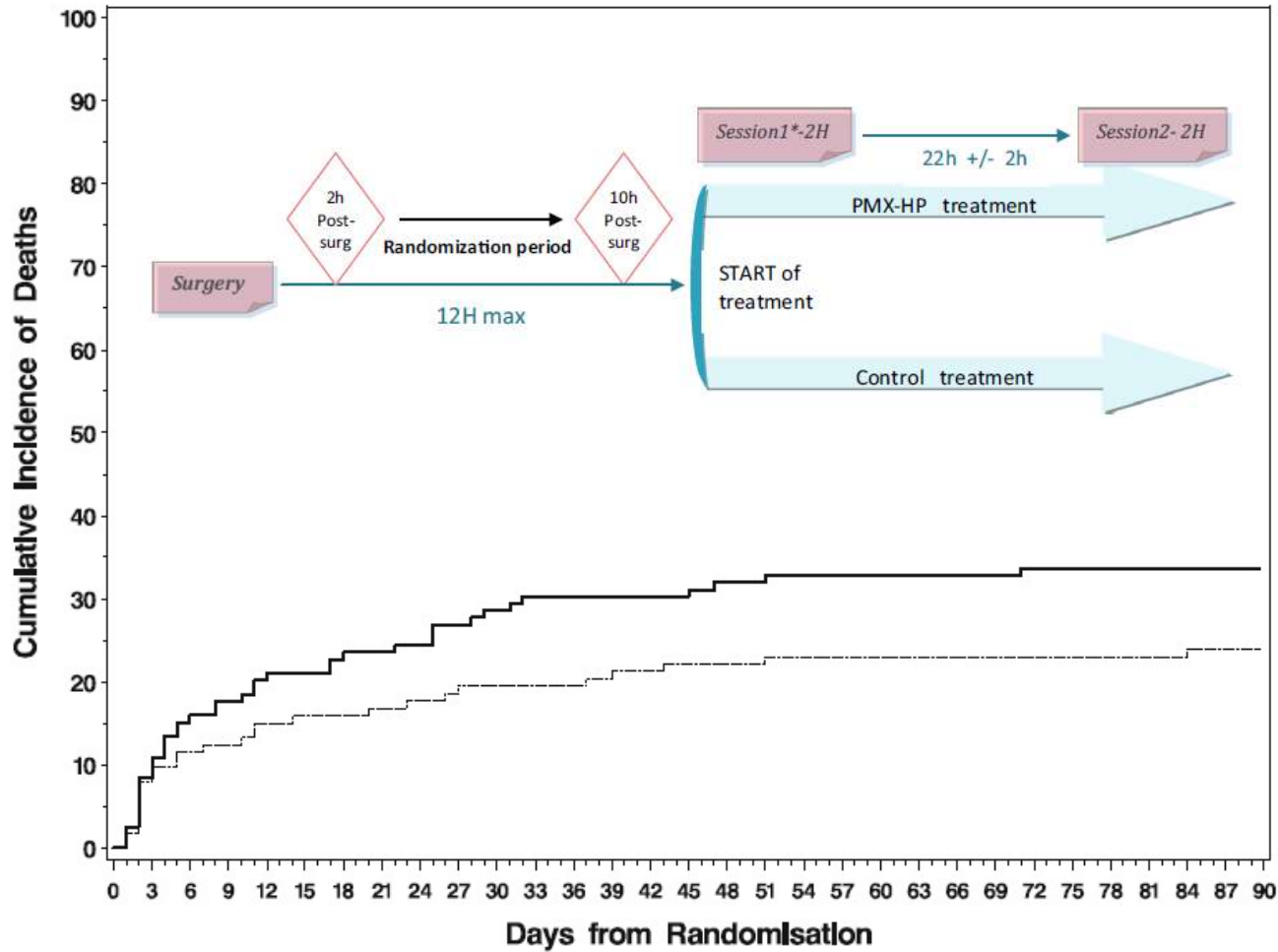
Sepsissterblichkeit in Deutschland höher als in anderen Ländern

In Deutschland wurde im Jahr 2015 laut dem Bündnis bei 320.198 Patienten eine Sepsis diagnostiziert, 23,1 Prozent von ihnen starben noch im Krankenhaus. 136.542 Menschen erhielten in dem Jahr die Diagnose „schwere Sepsis“. Die Mortalität in dieser Gruppe lag bei 41,2 Prozent. Sie liegt damit zehn bis 20 Prozent höher als zum Beispiel in Australien (18,5 Prozent), den USA (23,2 Prozent) und England (32,1 Prozent).

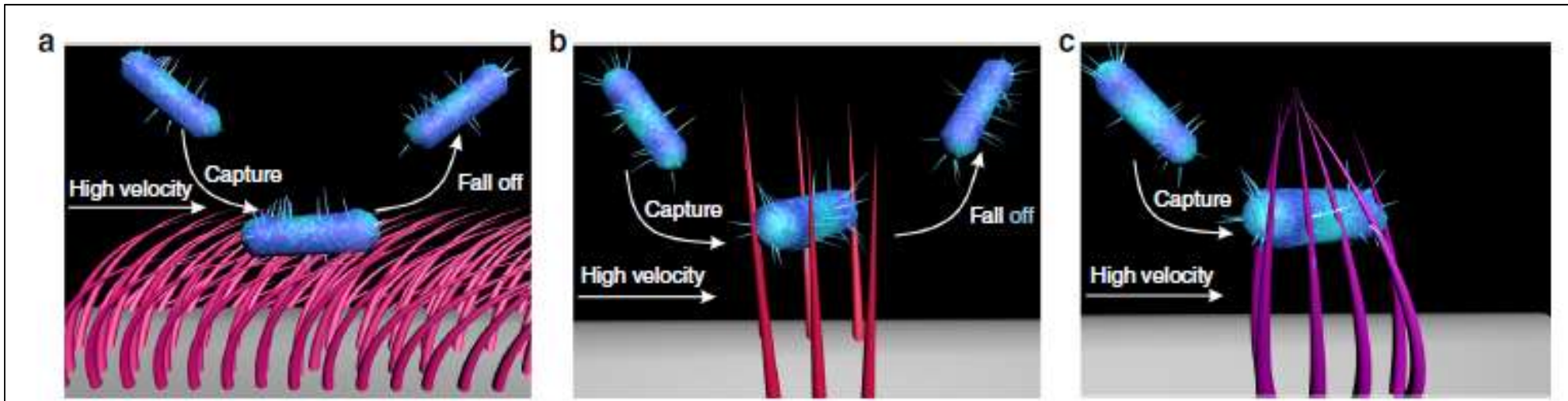
Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock



Early use of polymyxin B hemoperfusion in patients with septic shock due to peritonitis: a multicenter randomized control trial (n=243)



Bacterial capture efficiency in fluid bloodstream improved by bendable nanowires

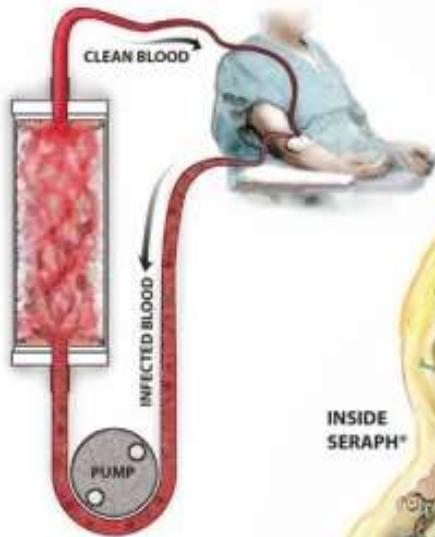


Seraph® Microbind® Affinity Blood Filter

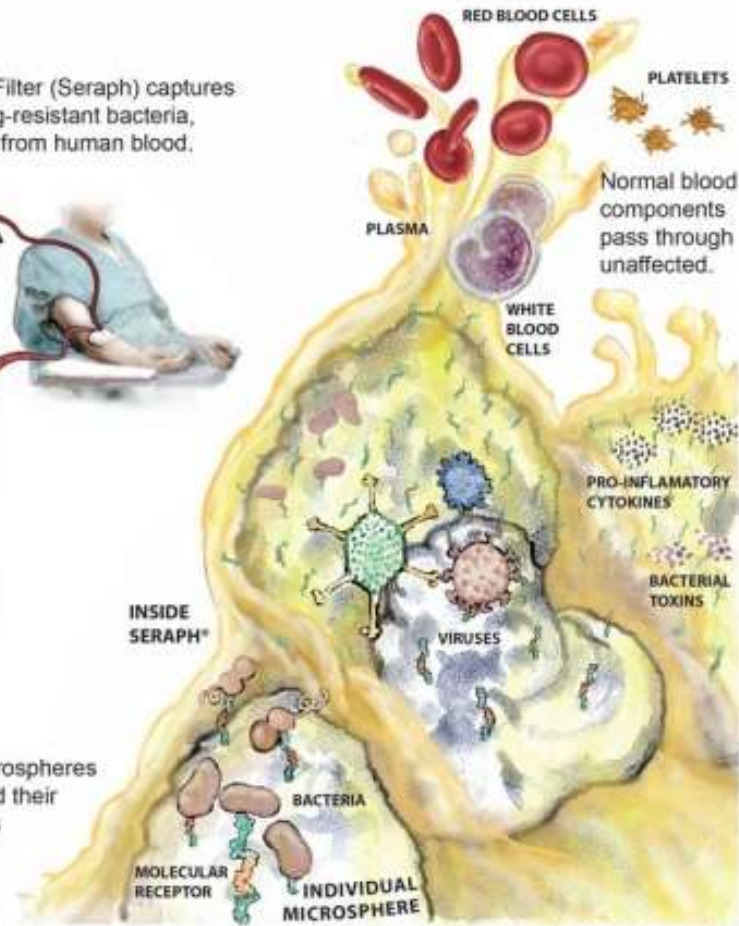
How Seraph works

ExThera's Seraph® Microbind® Affinity Blood Filter (Seraph) captures and removes a broad range of normal and drug-resistant bacteria, viruses, toxins and pro-inflammatory cytokines from human blood.

SINGLE-USE SERAPH® MICROBIND® AFFINITY BLOOD FILTER
Each cartridge is filled with proprietary 'microspheres' coated with molecular receptor sites that mimic the receptors on human cells used by pathogens when they invade the body.



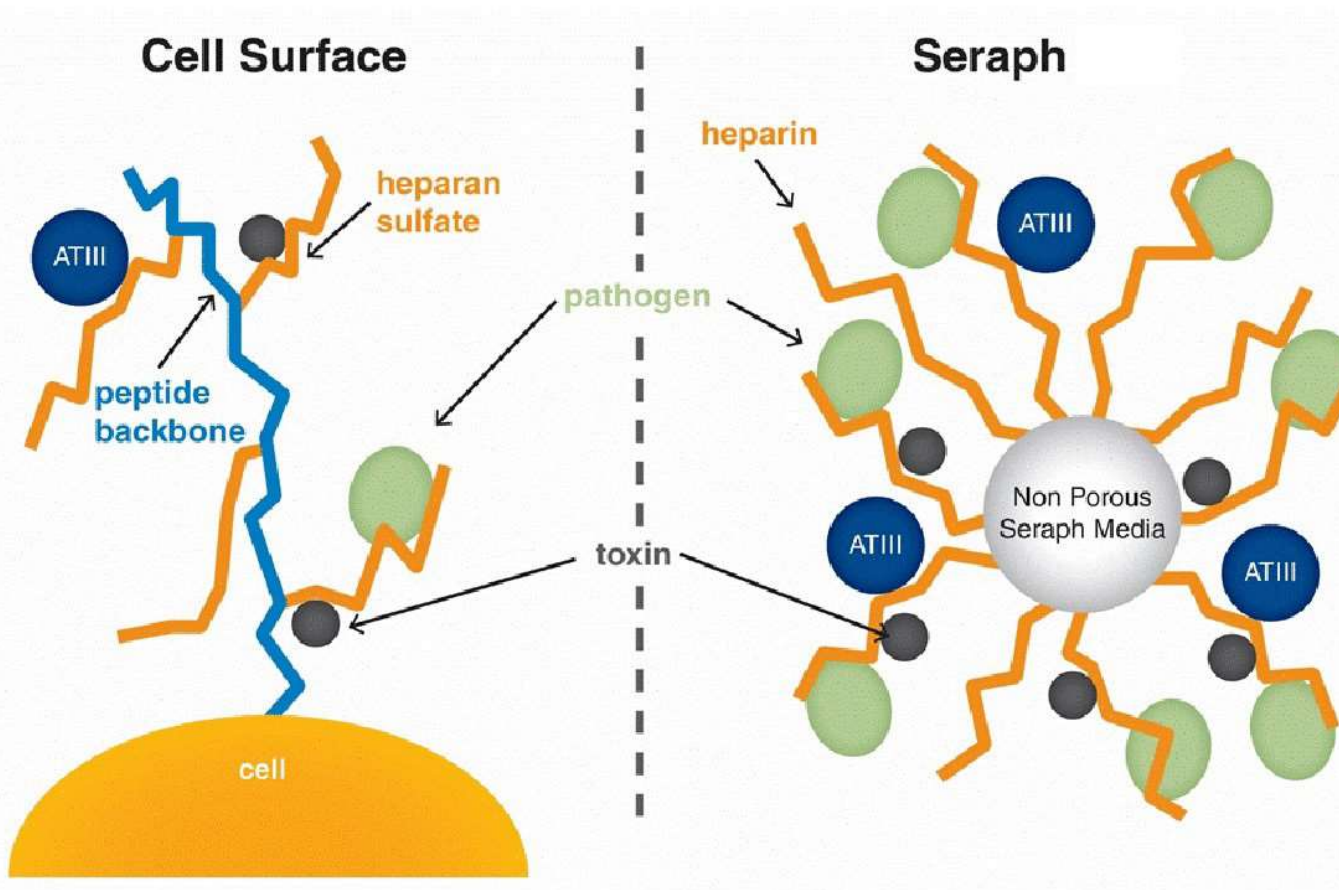
As blood flows between the microspheres in the filter bed, the invaders and their toxins bind to the surface just as they would in blood vessels within the body.



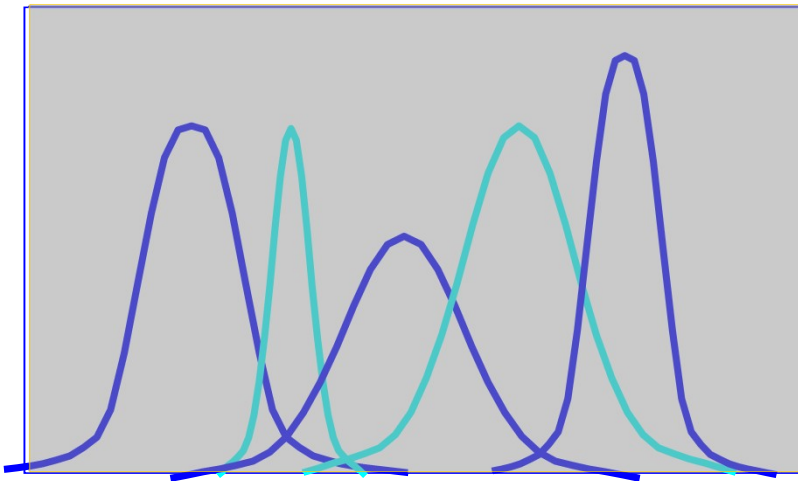
ExThera Medical Corporation - Berkeley, CA 94710 • info@extheramedical.com

NOTE: Drawing is for explanation only and is not to scale

High Affinity



Extracorporeal therapies in non-renal disease: treatment of sepsis and the peak concentration hypothesis

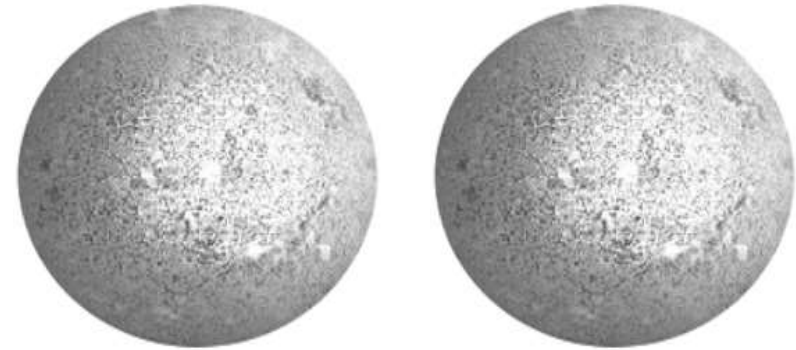


Excess □ pro- and □ anti-inflammatory mediators removed by continuous combined therapies

Unselective high efficiency extracorporeal therapies might remove excess of pro- and anti-inflammatory mediators diminishing the amplified inflammatory response and the immunoparalysis induced by cell hyporesponsiveness

A powerful new weapon in the fight against Cytokine Storm

biocompatible, highly porous polymer bead designed to capture and adsorb cytokines (~10-50 kDa)



Cytokine	Molecular weight	% removal
IL-8	8 kDa	100%
IL-1ra	17 kDa	100%
IL-1 α	17 kDa	100%
IL-10	18 kDa	85%
IL-6	26 kDa	87%
HMGB1	30 kDa	80%
TNF- α trimer	51 kDa	55%

Hemoadsorption by CytoSorb in septic patients: a case series (n=26)

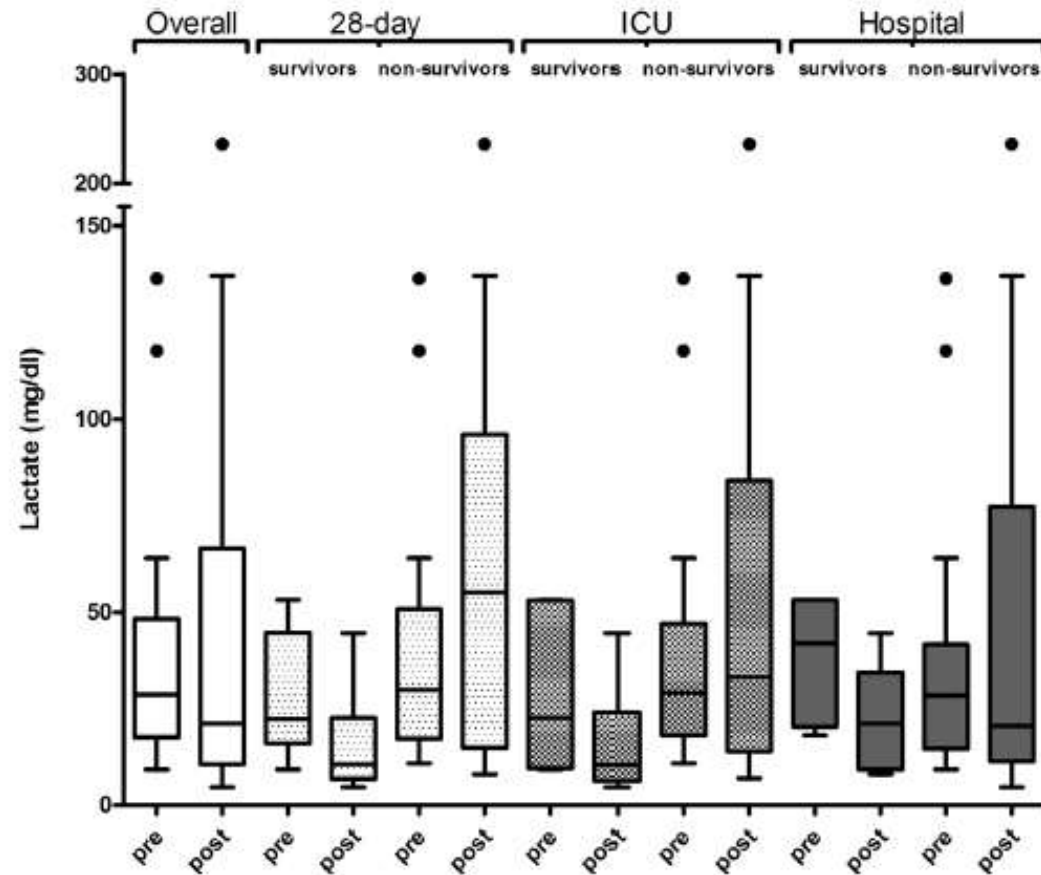


Fig. 2 Effect of CytoSorb hemoadsorption on blood lactate levels in relation to survival. Lactate levels (mg/dl) before (*pre*) and after (*post*) CytoSorb treatments in the overall patient population and in 28-day, ICU, and hospital survivors. In each *Tukey boxplot* the *whiskers* have equal lengths of 1.5 IQR. *Dots* represent outliers

Extracorporeal cytokine adsorption in septic shock: A proof of concept randomized, controlled pilot study (n=20)

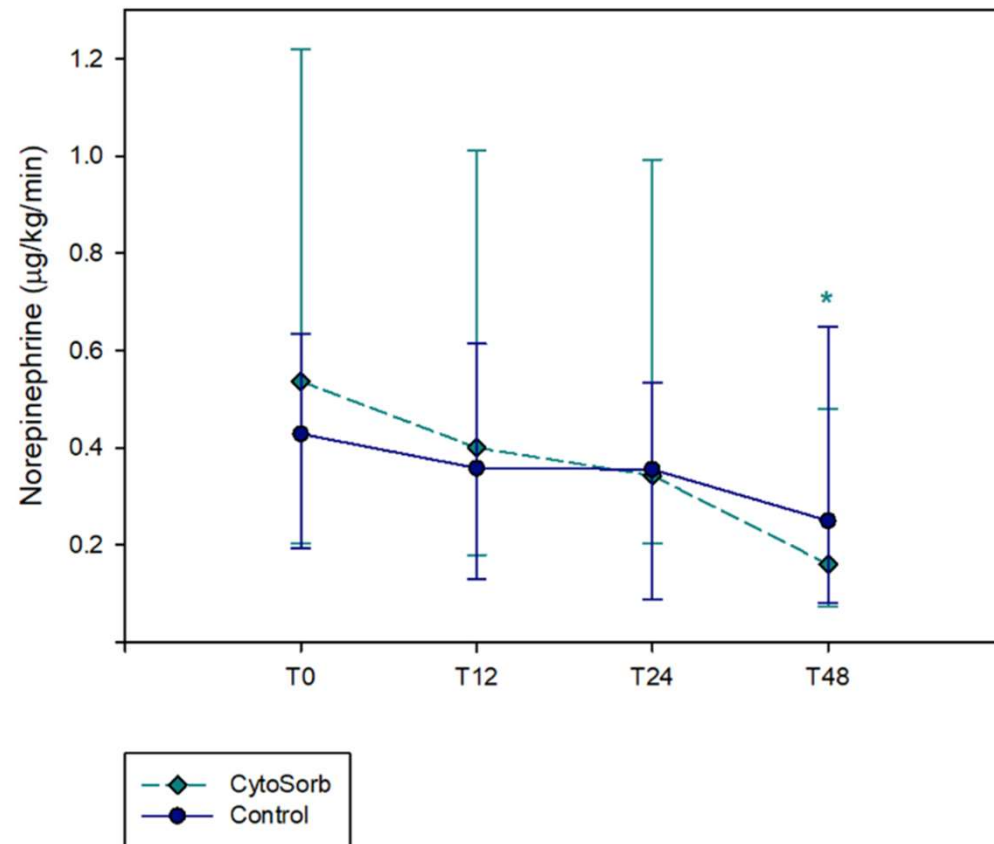


Fig. 2. Kinetics of norepinephrine need in the CytoSorb and in the Control group. Data are shown as median and interquartile ranges. * $p < .05$ vs. T_0 .

RESEARCH ARTICLE

Open Access

Therapeutic plasma exchange as rescue therapy in severe sepsis and septic shock: retrospective observational single-centre study of 23 patients

Johannes Hadem^{1*}, Carsten Hafer², Andrea S Schneider¹, Olaf Wiesner³, Gernot Beutel⁴, Thomas Fuehner³, Tobias Welte³, Marius M Hoeper³ and Jan T Kielstein²

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

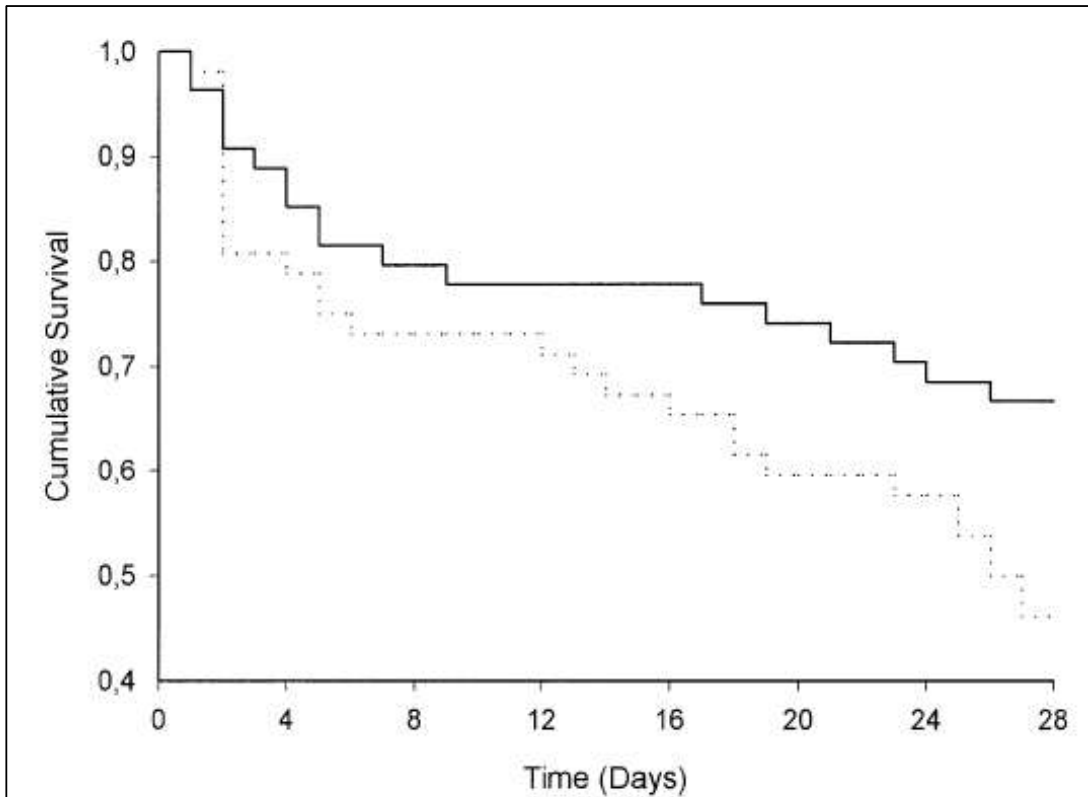


Fig. 1 Cumulative survival in 106 patients with severe sepsis or septic shock randomly assigned to plasmapheresis (*solid line*) or not (*dotted line*) in addition to standard sepsis treatment

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

Table 4 Multiple logistic regression analysis evaluating the adjusted effects of unbalanced baseline characteristics and plasmapheresis on mortality in patients with severe sepsis or septic shock

Independent variable	Odds ratio	95% CI	<i>p</i>
Age (10 years) ^a	1.48	1.03–2.12	0.03
Site of infection			0.04
Abdominal	Reference		
Female genital	0.54	0.07–4.00	
Urological	0.15	0.02–0.93	
Lung	4.04	0.74–22.2	
Skin/soft tissue	0.41	0.07–2.53	
Brain	1.60	0.30–8.62	
Other	1.71	0.33–8.88	
Plasma exchange	0.41	0.15–1.09	0.07

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue

Sepsis with multi-organ failure

TPE

III

2B

TABLE II. Category Definitions for Therapeutic Apheresis

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

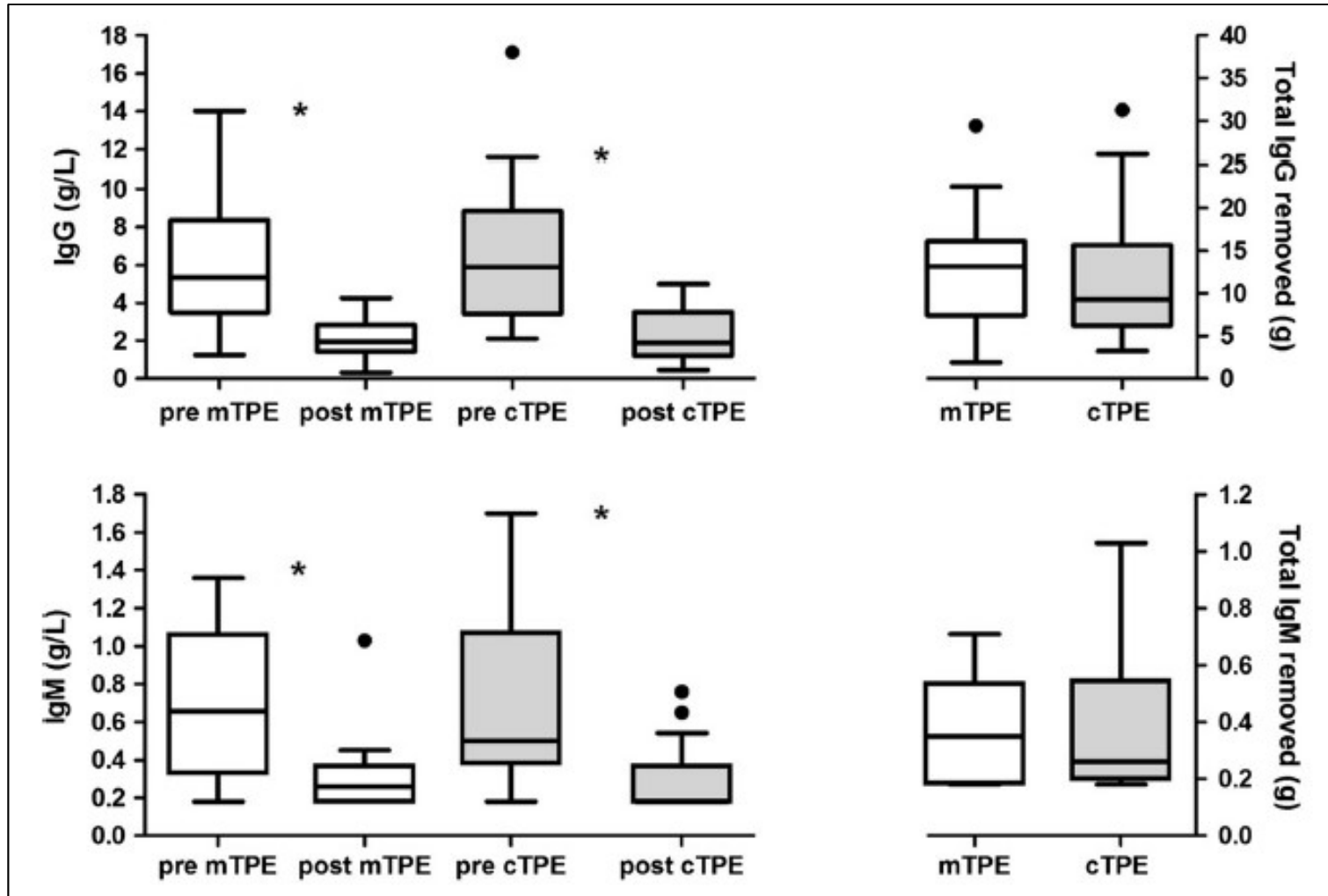
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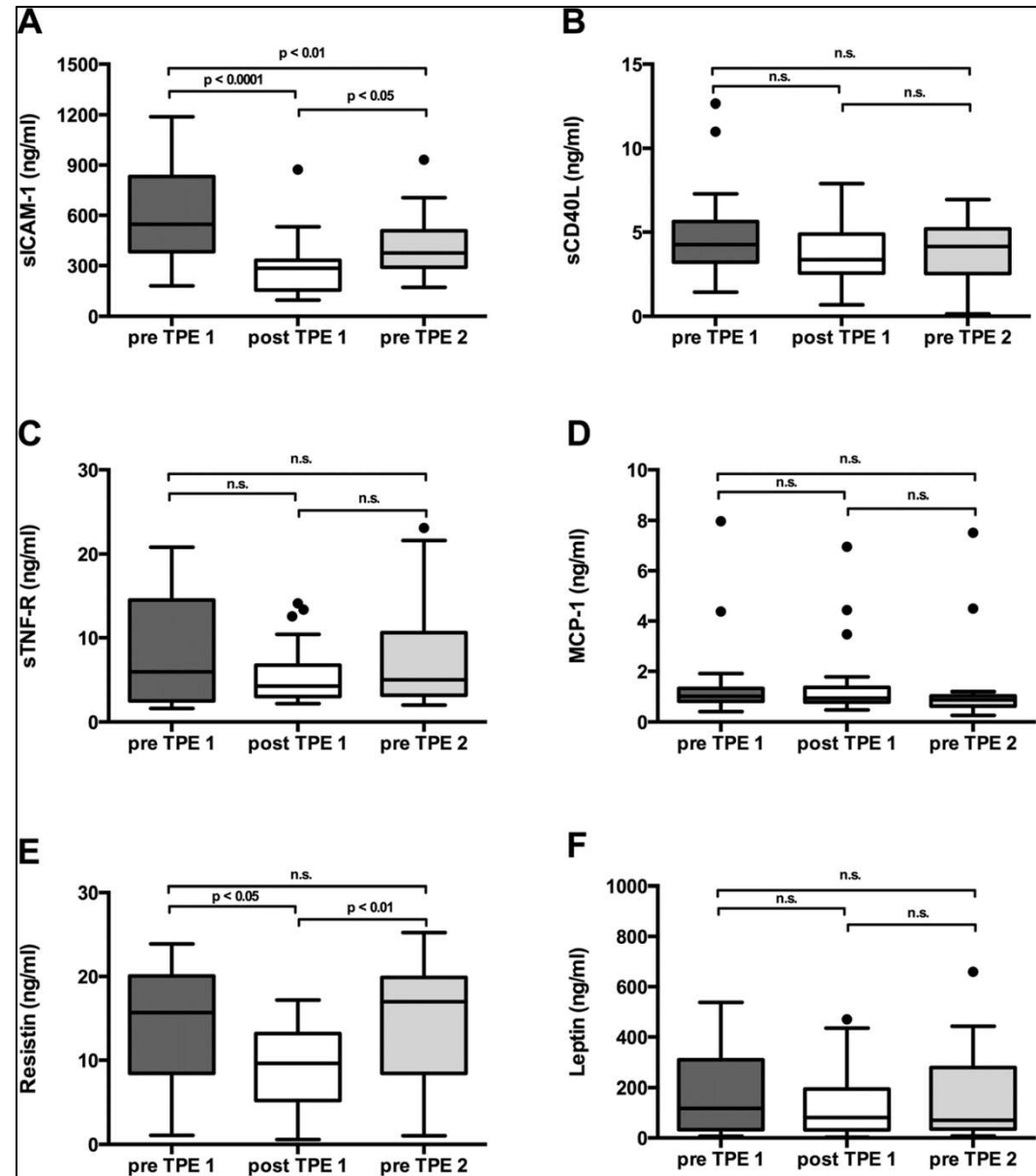
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Membrane vs centrifuge-based TPE: a randomized prospective crossover study



Effect of TPE on plasma levels and total removal of adipokines and inflammatory markers

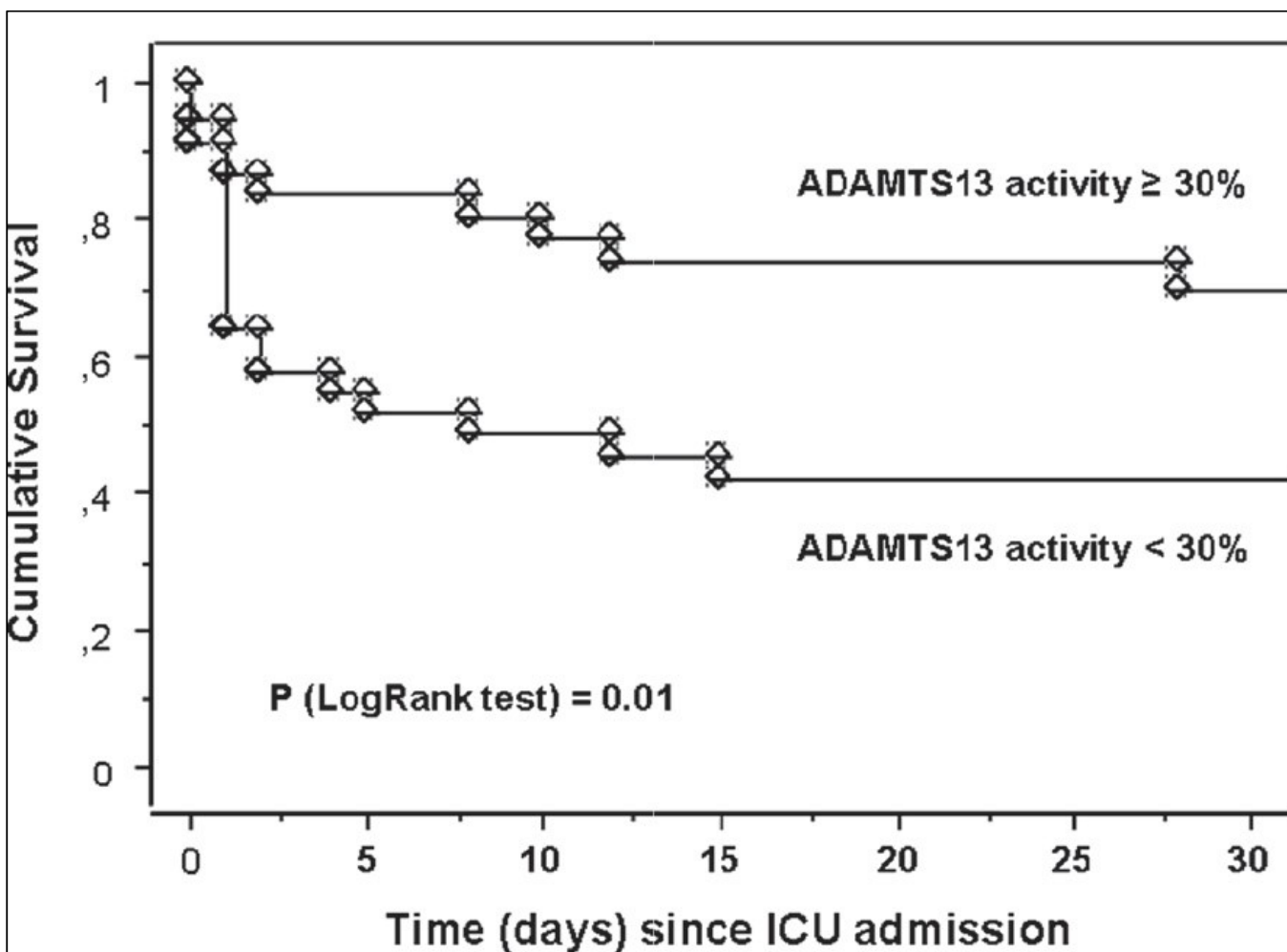


Rolle von Plasmapherese und Immunadsorption in der Rescue-Therapie rheumatologischer Erkrankungen

Tab. 1 Was entfernt die Plasmapherese (PE)?

Substanz	Reduktion Prä- vs.- Post-PE (%)	Entfernte Menge	Ausgetauschtes Plas- mavolumen (PV)	Referenz
IgG	65	12,3 ± 1,1 g (SEM)	1,2-faches PV	[3]
IgM	54	0,39 ± 0,04 g (SEM)	1,2-faches PV	[3]
CRP	64	~10 mg	1,2-faches PV	[7]
sICAM-1	50	1,3 ± 0,9 mg	1,2-faches PV	[5]
	45	210,2 ± 20,3 ng/ml	1,0-faches PV	[6]
sTNF-R	30	21,3 ± 18,6 µg	1,2-faches PV	[5]
IL-1β	+8	3,12 ± 0,15 pg/ml	1,0-faches PV	[6]
IL-1ra	+62	1020 ± 210 pg/ml	1,0-faches PV	[6]
IL-8	+92	205,2 ± 75,6 pg/ml	1,0-faches PV	[6]
VCAM-1	45	710,4 ± 40,0 pg/ml	1,0-faches PV	[6]

The prognostic value of ADAMTS13 deficiency in septic shock patients involves interleukin-6 and is not dependent on disseminated intravascular coagulation



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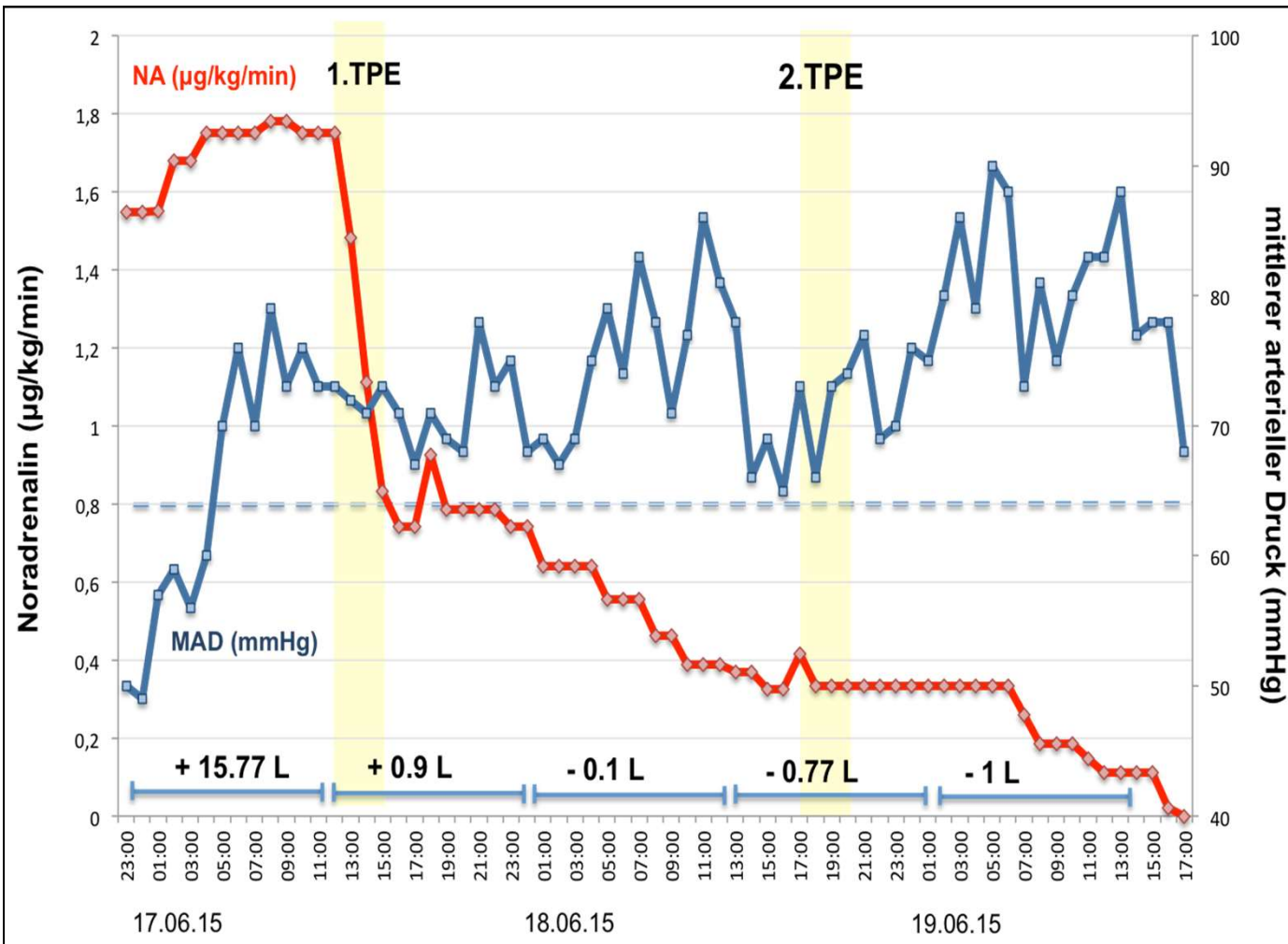
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Andre A. Kaplan



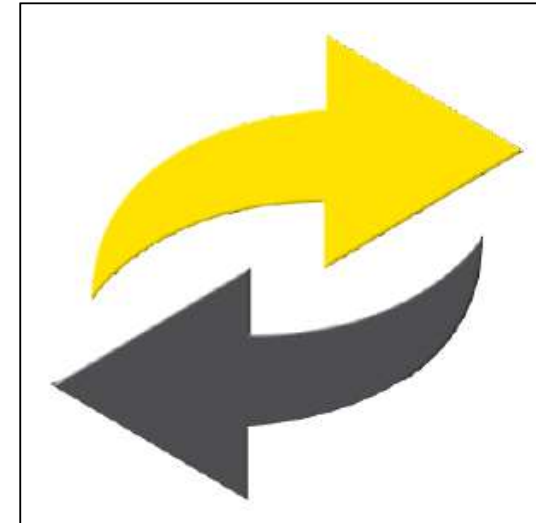
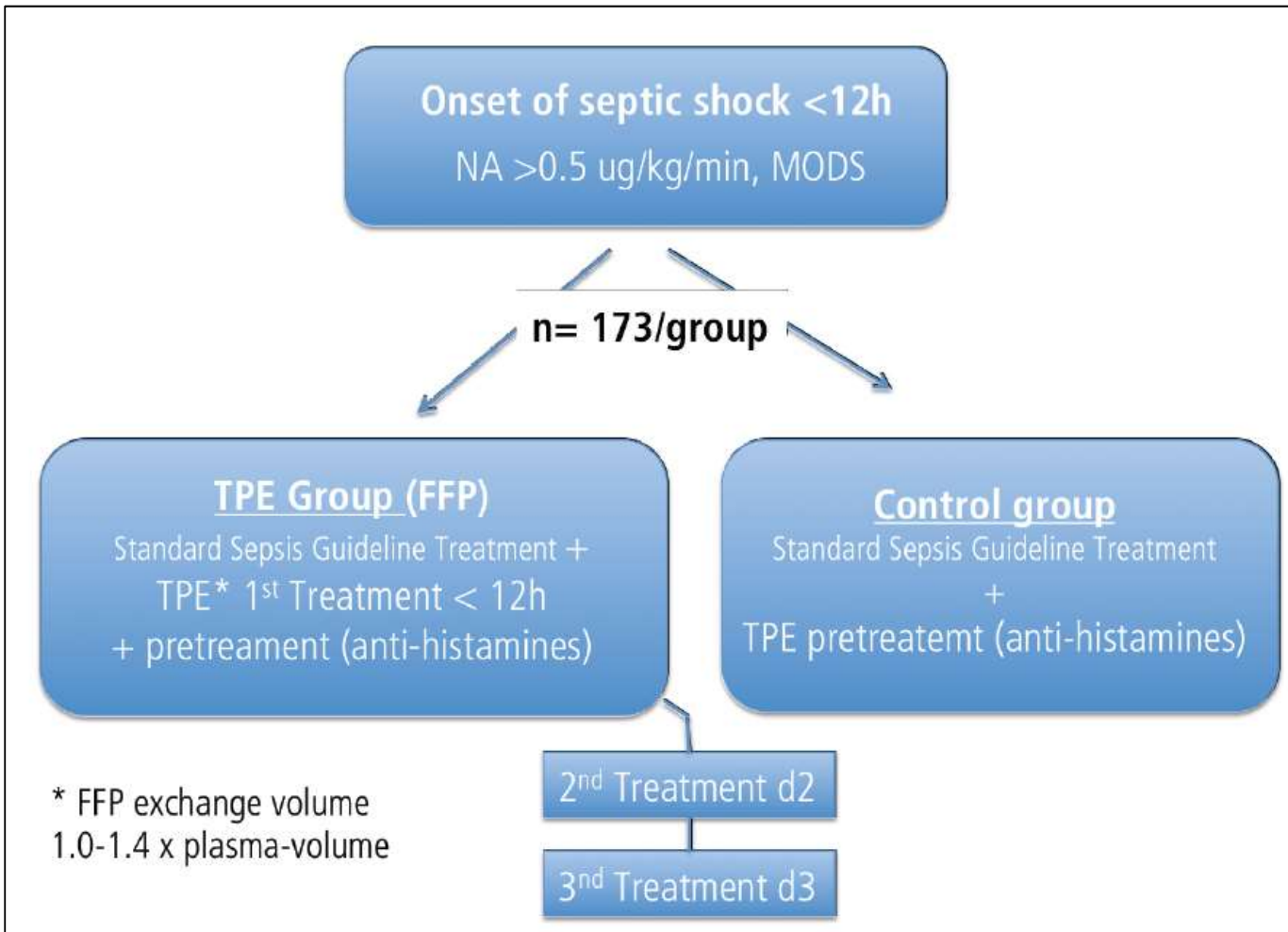
**“Nobody in the ICU
should die without
plasma exchange”**

Plasma exchange in treatment refractory septic shock : Presentation of a therapeutic add-on strategy

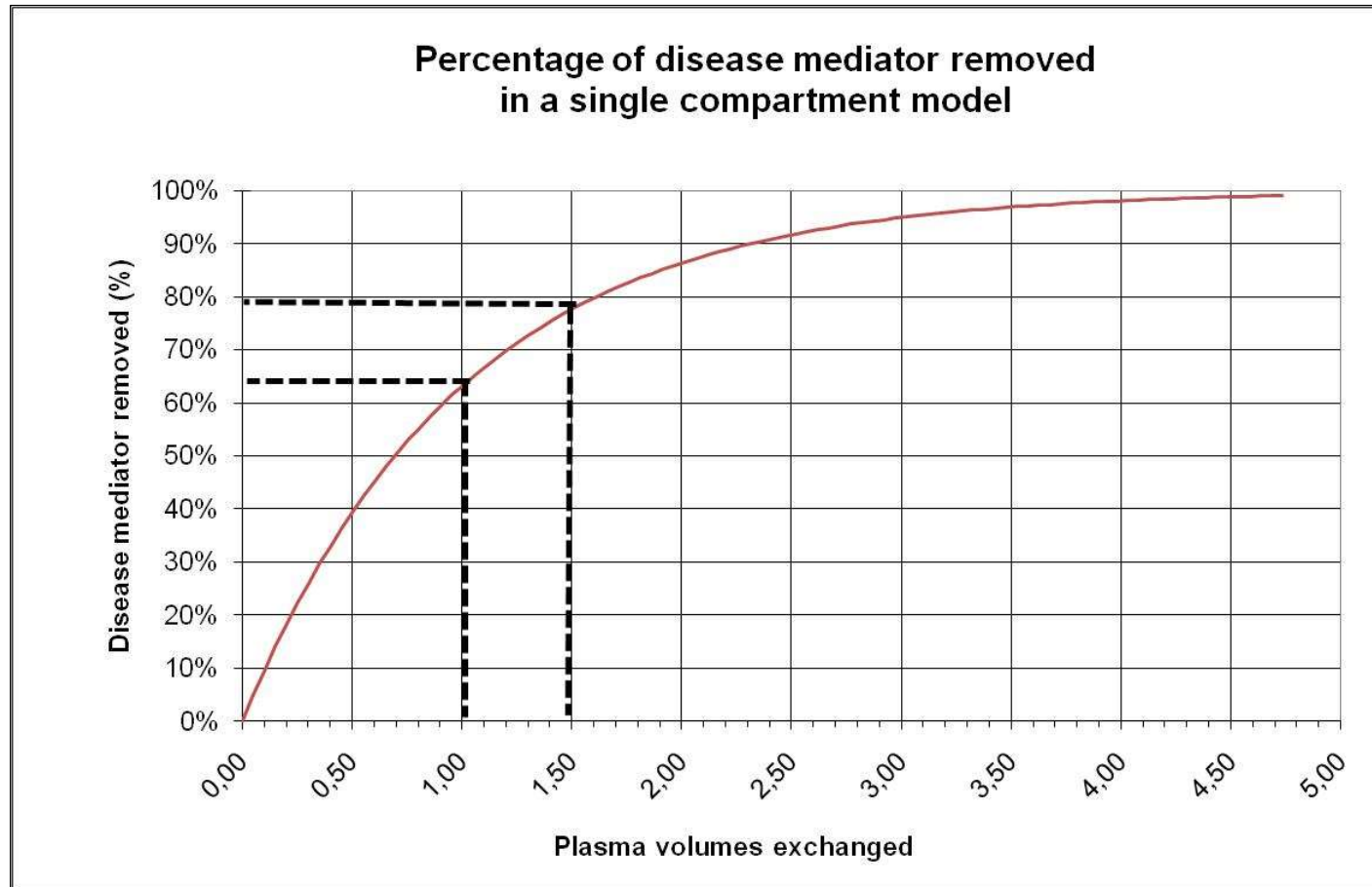


Plasmaexchange in Early Septic Shock (EXCHANGE)

www.clinicaltrials.gov NCT03065751

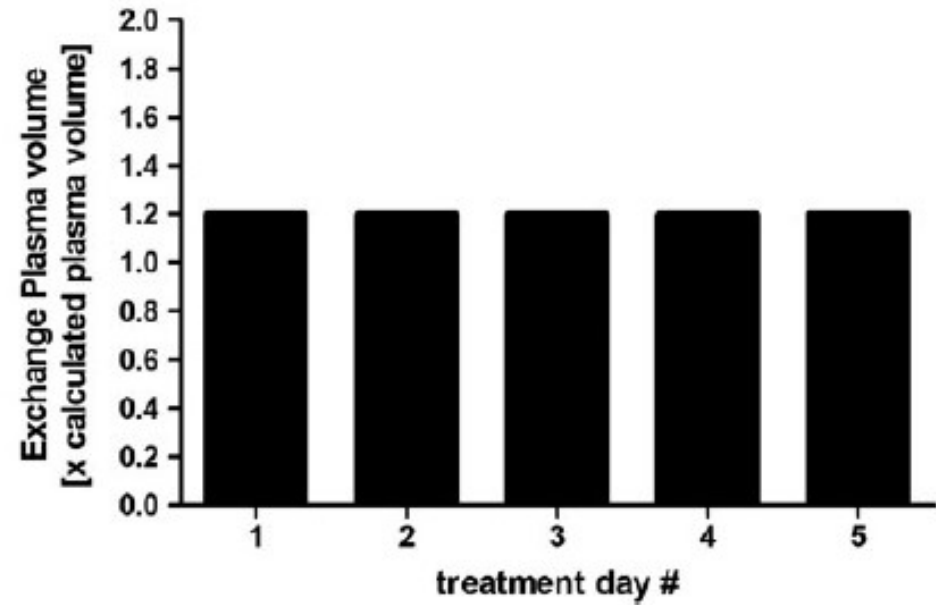
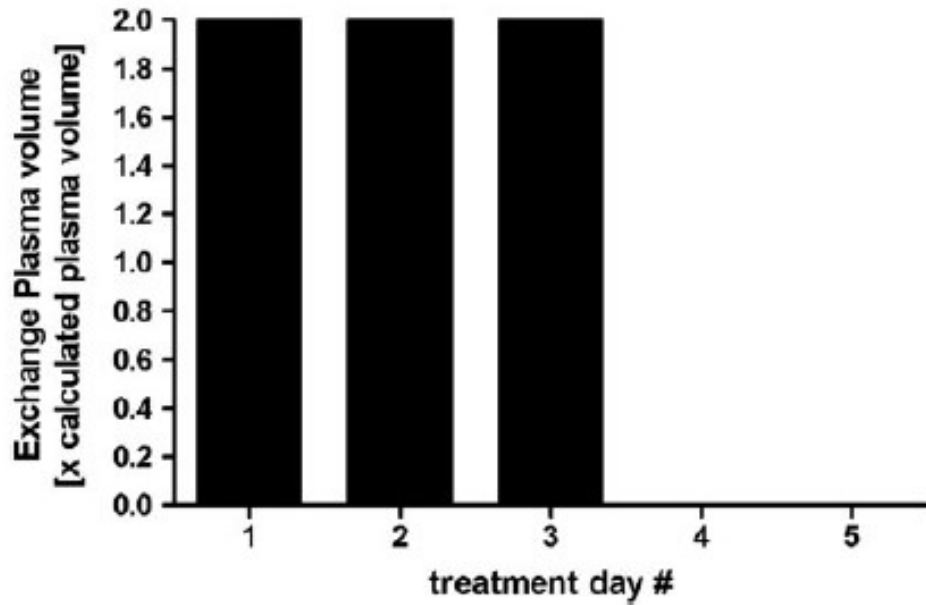


A simple and accurate method for prescribing plasma exchange

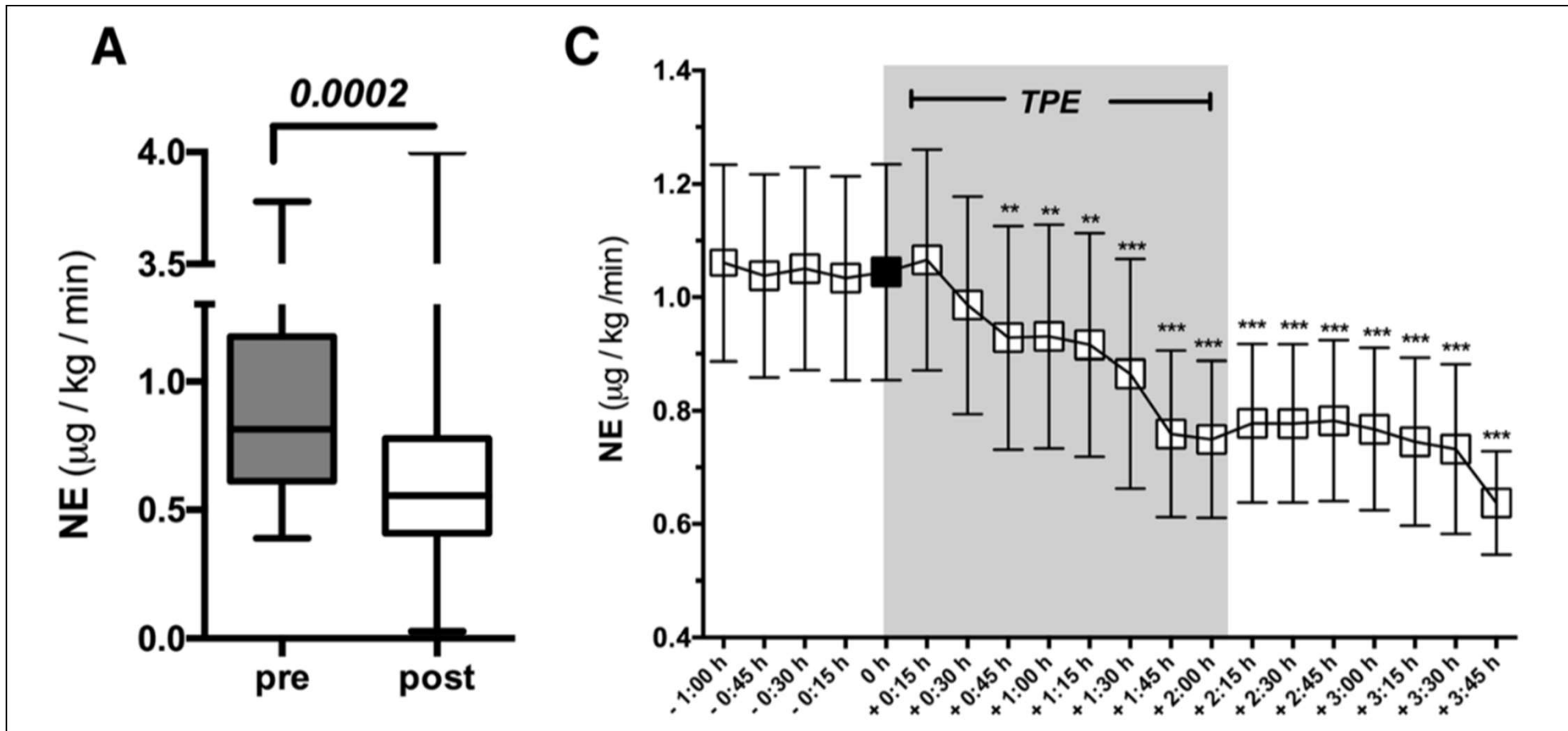


$$EPV = [0.065 \times wt(kg)] \times [1-Hct]$$

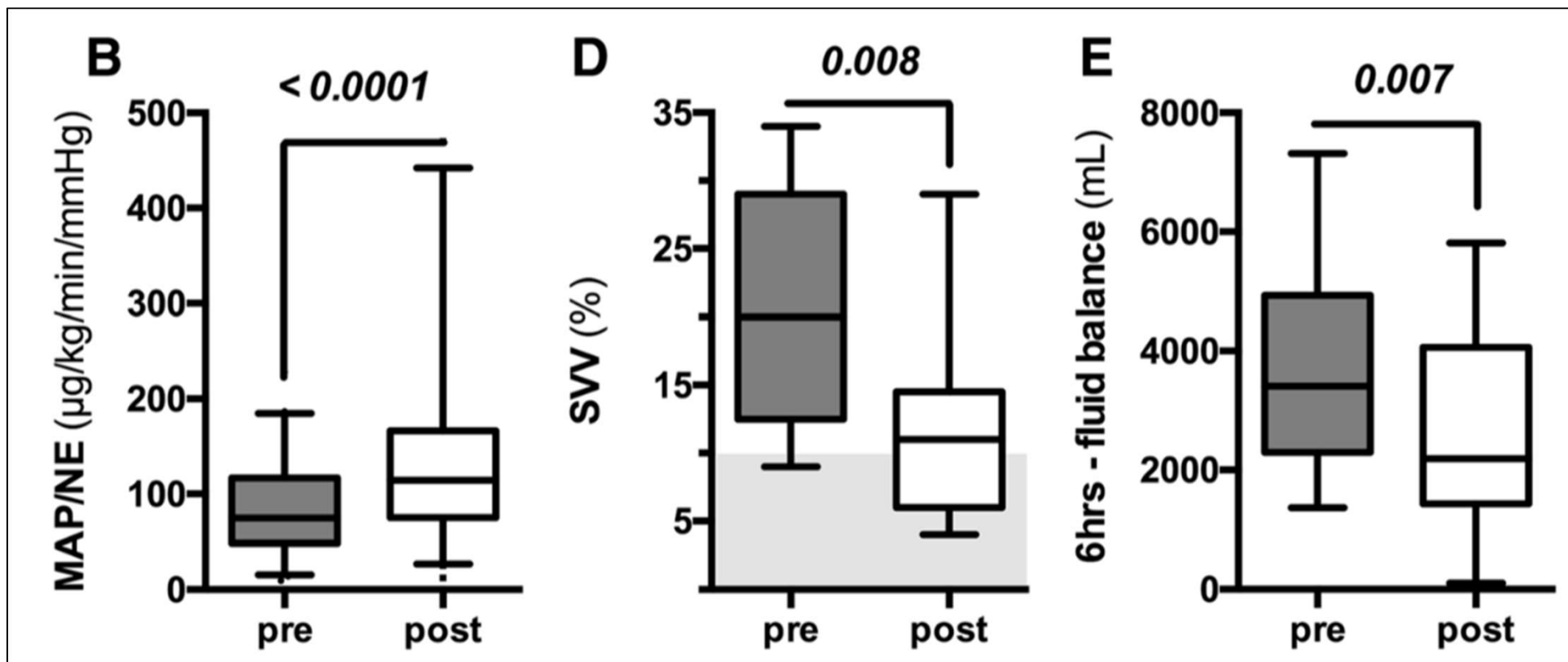
Pro: High dose of therapeutic plasma exchange-mind the gap!



Early therapeutic plasma exchange in septic shock: a prospective open-label nonrandomized pilot study focusing on safety, hemodynamics, vascular barrier function, and biologic markers



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