Hemoadsorption in Cardiac Surgery and Infective Endocarditis

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Conflict of Interest

* Edwards Lifesciences Clinical Events Committee
* CytoSorbents

Outline

1. The History
2. The Evidence over Time
3. The Technical Aspects
4. Current Knowledge
5. Conclusions

The inflammation

The Inflammation

* Non-specific response against aggressions from the environment
* Generated by inflammatory agents
* Occurs only in vascularized tissues
* To isolate and destroy the invasive agent
* To repair the damaged tissue or organ

From Roman Latin: To make fire

What we do in practice

Cardiovascular Surgery

We create inflammation

The Facts

* Arteriolar and capillary vasodilation (5HT + NO)
* Increase in arteriolar blood flow velocity (Hyperemia)
* Increase microvascular permeability (Edema)
* Abnormal blood pooling (Increased blood viscosity – venous congestion)
* Blood stasis in microvessels
* Peripheral leucocyte pooling
* Activation of endothelial cells (PMN)
* PNM + Macrophage migration into interstitial space (Diapedesis)

* Trauma to tissues

* Manipulation of blood vessels

* Disruption of endothelial lining

* Blood exposed to artificial surface (Silicone, Tygon,…)

* …

The Inflammation in Cardiac Surgery

SIRS

Major surgery

IL-6>200 pg/ml - SIRS

IL-6>300 pg/ml- Increased risk of pneumonia, MOF and death in trauma patients

The main goal of therapy is the removal of inflammatory mediators from the patient's blood

* **Cytokines**
* **Chemokines**

* Cytokines are glycoproteins that regulate the functions of the immune system

* Definitions are imprecise because of redundancy of function and the capacity of tissue parenchymal cells and leukocytes to produce them

* Lymphokine/monokine are no longer in use
Originally described by their perceived major function, the term IL has been adopted

* When a cytokine is broadly accepted, a number is attributed (eg, IL-6).

Holdsworth SR, Gan PY. Clin J Am Soc Nephrol 2015; 10:2243-2254

Descriptive names for some key cytokines

* IFNs (α, β, and γ)
* TNF (TNF-α and TNF-β)
* Colony stimulating factors
    - Granulocyte colony–stimulating factor [G-CSF]
    - Granulocyte–macrophage colony–stimulating factor [GM-CSF])
    - Growth factors (TGF-β and PDGF)

Outline

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JECT. 2009;41:149–156
The Journal of ExtraCorporeal Technology

Original Articles

Clinical Efficacy of Two-Phase Leukocyte Filtration in High-Risk Patients Undergoing Coronary Revascularization with Cardiopulmonary Bypass

Serdar Gunaydin, MD;* Thomas Modine, MD;† Tamer Sari, MSc;‡ Yaman Zorlutuna, MD;‡ Terence Gourlay, PhD§

*Department of Cardiovascular Surgery, University of Kirikkale, Kirikkale, Turkey; †Hôpital Cardiologique, CHRU de Lille, Lille, France; ‡Bayindir Hospital, Ankara, Turkey; and §Bioengineering Unit, University of Strathclyde, Glasgow, Scotland

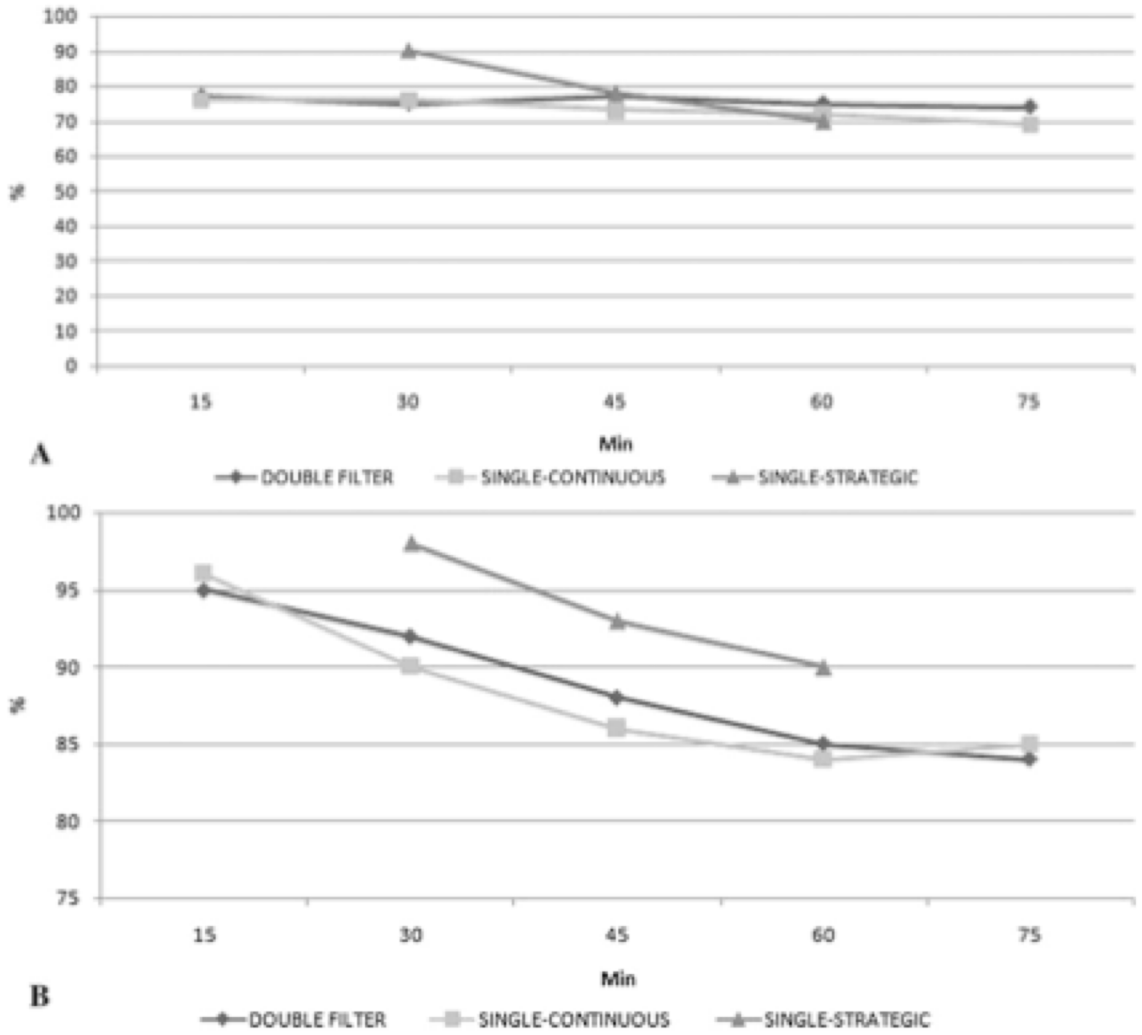


Figure 5. Percent reduction of neutrophils (A) and platelets (B) through leukofilters during CPB. *<.05 vs. control (group 4), ‡<.05 vs. group 2, and ¶<.05 vs. group 3.

Steroid Administration in Heart and Heart–Lung Transplantation: Is the Timing Adequate?

Song Wan, MD, Jean-Marie DeSmet, MD, Martine Antoine, MD,
Michel Goldman, MD, PhD, Jean-Louis Vincent, MD, PhD, and Jean-Louis LeClerc, MD

Departments of Cardiac Surgery, Immunology and Intensive Care, University Hospital Erasme, Free University of Brussels, Brussels, Belgium

(Ann Thorac Surg 1996;61:674–8)

Routine administration of corticosteroids before cardiopulmonary bypass (CPB) has been used for many years [16], although the beneficial effect of this intervention has not been proven. Recent studies have indicated that steroid administration before CPB may prevent the release of TNF-α [17] and IL-8 [18, 19], or increase the production of IL-10 [19]. This cytokine response may be involved in the development of complications after CPB,

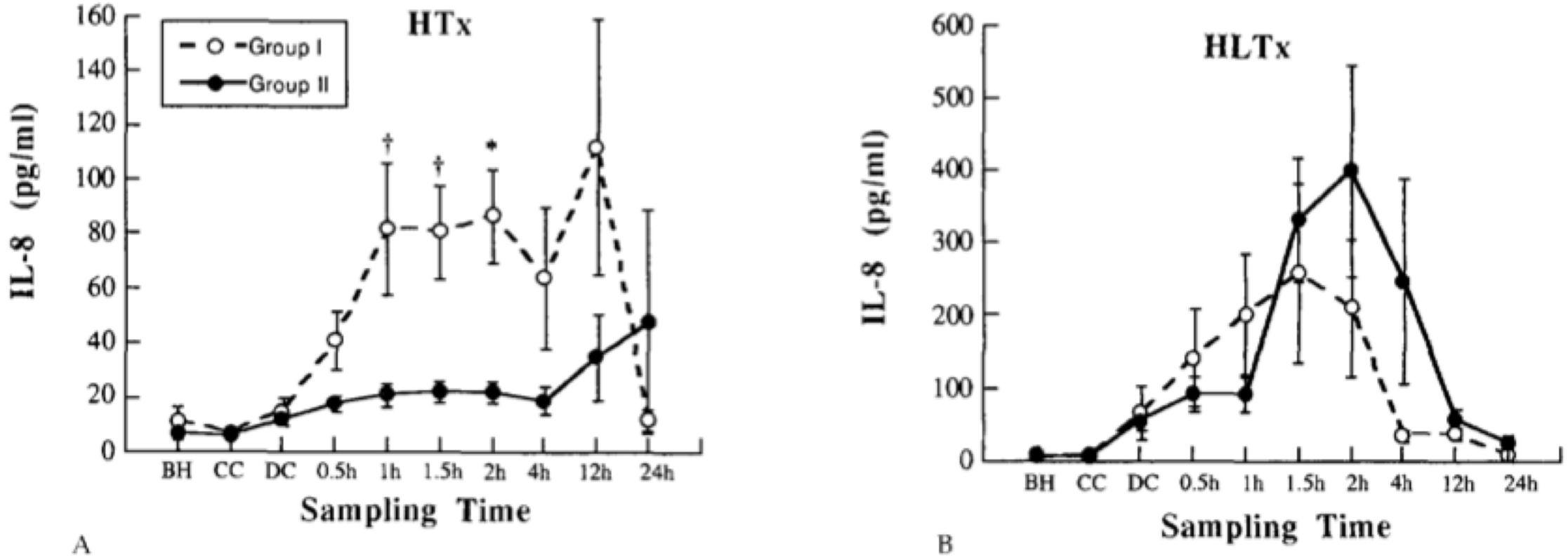


Fig 2. Plasma interleukin-8 (IL-8) levels in heart transplant (HTx) patients (A) and in heart–lung transplant (HLTx) patients (B). See legend of Figure 1 for details.

In summary, earlier steroid administration can reduce the inflammatory response to CPB in patients undergoing HTx or HLTx, as reflected by a lower production of TNF-α and IL-8, but a greater release of IL-10. Earlier administration of steroids in HTx or HLTx patients may be preferable to reduce the postoperative complications and to improve the immune response to transplantation. Our study included only one dose regimen of steroids before CPB. Higher doses of steroids may have better inhibitory effects. Further investigation is certainly warranted.

HUMAN CYTOKINE RESPONSES TO CARDIAC TRANSPLANTATION AND CORONARY ARTERY BYPASS GRAFTING

Cardiac surgery with cardiopulmonary bypass triggers an inflammatory response involving proinflammatory cytokines such as tumor necrosis factor-α, interleukin-6, and interleukin-8. To elucidate the pathophysiology of this cytokine response, we explored the possible differences in cytokine responses between patients undergoing heart transplantation and those undergoing coronary artery bypass grafting. Plasma levels of tumor necrosis factor-α, interleukin-6, interleukin-8, and interleukin-10 were measured in eight patients undergoing heart transplantation (mean age 44 years) and eight patients undergoing coronary artery bypass grafting

Song Wan, MD,[a] Arnaud Marchant, MD,[b] Jean-Marie DeSmet, MD,[a] Martine Antoine, MD,[a] Haibo Zhang, MD, PhD,[c] Jean-Luc Vachiery, MD,[d] Michel Goldman, MD, PhD,[b] Jean-Louis Vincent, MD, PhD,[c] and Jean-Louis LeClerc, MD,[a] *Brussels, Belgium*

J THORAC CARDIOVASC SURG 1996;111:469-77

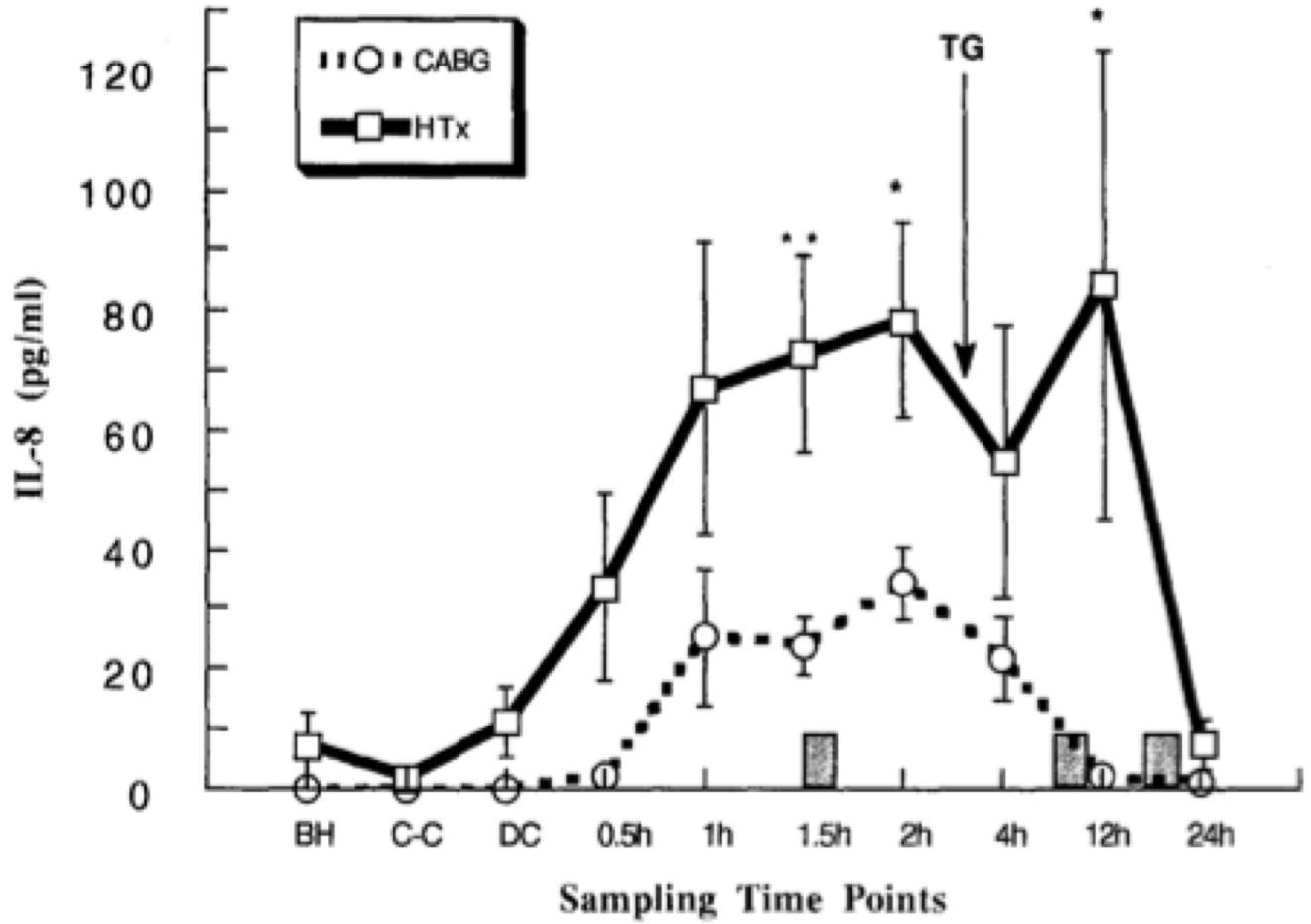


Fig. 4. Plasma IL-8 levels in the HTx ($n = 8$) and CABG ($n = 8$) groups. *Asterisk* indicates $p < 0.05$ vs CABG group; *double asterisk* indicates $p < 0.01$ vs CABG group. Data are mean ± SEM. *BH,* Before heparin administration; *C-C,* crossclamping; *DC,* declamping; *TG,* thymocyte immunoglobulin. *Shaded bars* indicate steroid administration in HTx group.

In conclusion, the elevation of the levels of proinflammatory cytokines TNF-α, IL-6, IL-8 are shown to be more pronounced in patients undergoing HTx than those undergoing CABG, and these differences are related at least in part to a longer duration of ischemia in the HTx group. Our study also indicates that antiinflammatory cytokine IL- 10 is released during and after CPB, and that the degree of release of IL-10 is not related to the duration of ischemia. In the HTx group, the cytokine responses may also have been influenced by immunosuppressive therapy. Whether anticytokine strategies aiming at a reduction in reperfusion injury can reduce complications after CPB is an intriguing question that remains open.

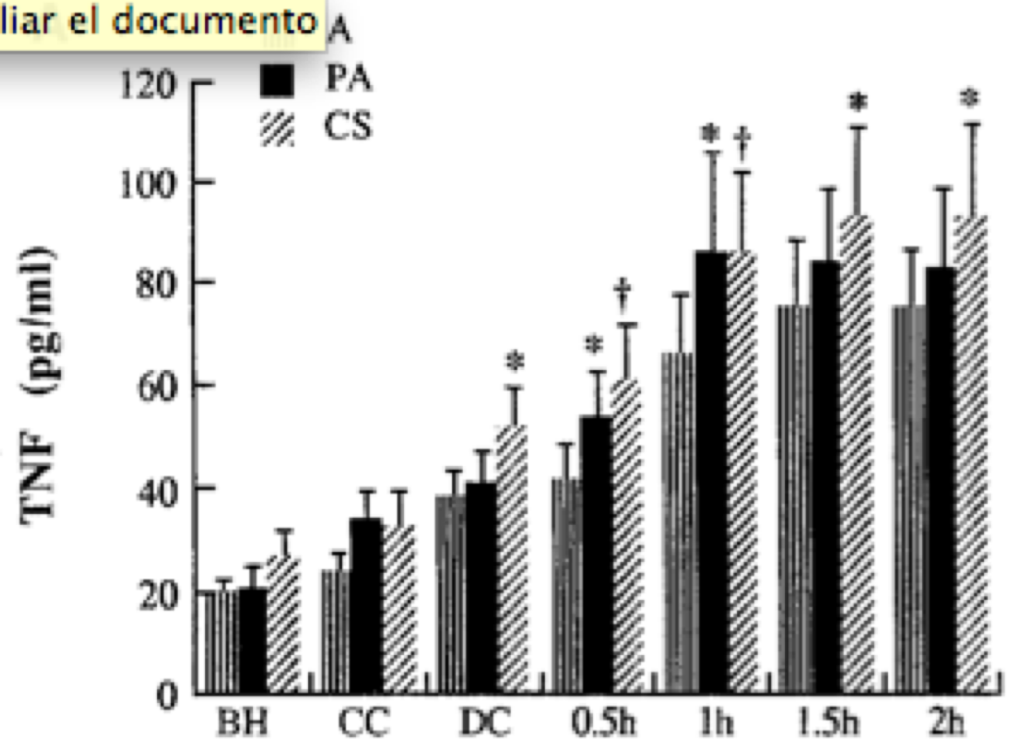
MYOCARDIUM IS A MAJOR SOURCE OF PROINFLAMMATORY CYTOKINES IN PATIENTS UNDERGOING CARDIOPULMONARY BYPASS

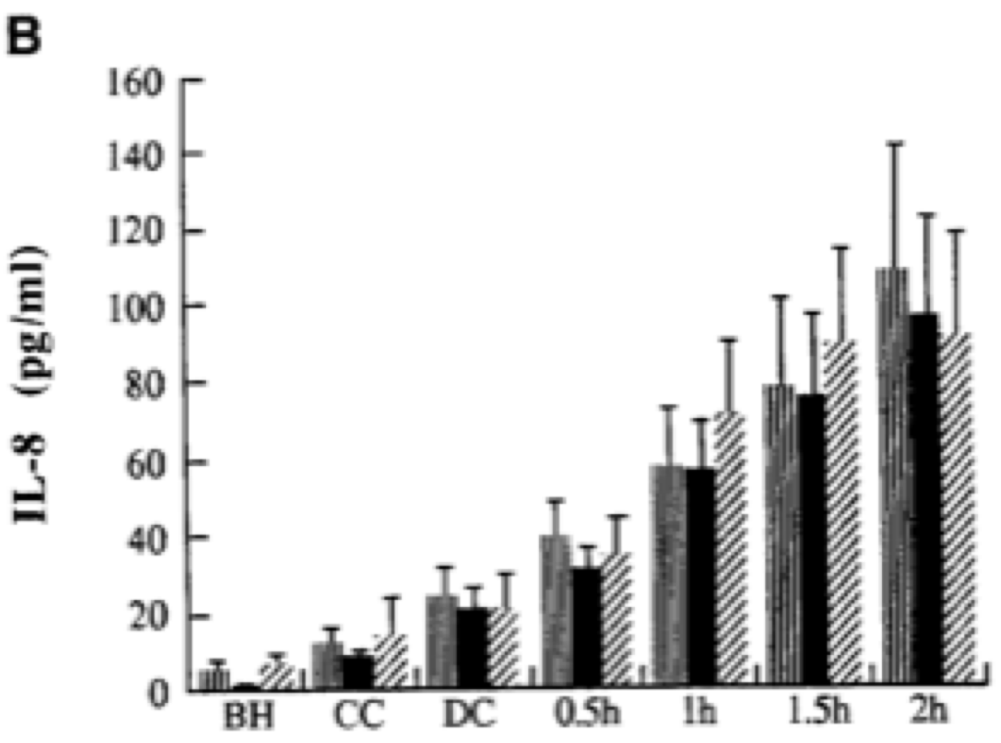
Song Wan, MD[a]
Jean-Marie DeSmet, MD[a]
Luc Barvais, MD[b]
Marcelo Goldstein, MD[c]
Jean-Louis Vincent, MD, PhD[c]
Jean-Louis LeClerc, MD[a]

Proinflammatory cytokines, such as tumor necrosis factor–α, interleukin-6, and interleukin-8, and antiinflammatory cytokines, such as interleukin-10, may play an important role in patient responses to cardiopulmonary bypass. We sought to define whether the myocardium and the lungs serve as important sources of these cytokines under conditions of cardiopulmonary bypass. Ten patients (age 64 ± 3 years, mean ± standard error of the mean) undergoing elective coronary artery bypass grafting were monitored with an arterial catheter, a coronary sinus catheter, and a pulmonary artery catheter. Plasma levels of tumor necrosis factor–α, interleukin-6, interleukin-8, and interleukin-10 were measured simultaneously in peripheral arterial blood, coronary sinus blood, and mixed venous blood before heparin administration, 1 minute

J Thorac Cardiovasc Surg 1996;112:806-11

Ampliar el documento





In summary, this study demonstrates that the heart, not the lungs, is a major source of the proinflammatory cytokines TNF-α and IL-6 after reperfusion of ischemic myocardium in patients undergoing CPB. The lungs may even consume these proinflammatory cytokines under such conditions. Neither the heart nor the lungs are the main source of the antiinflammatory cytokine IL-10.

Cytokine Responses to Cardiopulmonary Bypass: Lessons Learned From Cardiac Transplantation

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Background. A growing body of evidence relates the release during cardiopulmonary bypass (CPB) of proinflammatory cytokines, such as tumor necrosis factor-α, interleukin (IL)-6, and IL-8, to the postoperative systemic inflammatory response syndrome. Antiinflammatory cytokines, such as IL-10, however, may also play an important role in limiting these complications.

Methods. The English-language literature was reviewed. Emphasis was placed on cytokine responses during clinical CPB for cardiac operations and, in particular, for heart and heart-lung transplantation.

Results. The recent data indicate that (1) although cytokine release can be triggered by many factors during CPB, ischemia-reperfusion may play the most important role; (2) the levels of tumor necrosis factor-α, IL-6, and IL-8 are correlated with the duration of cardiac ischemia and the myocardium is a major source of these three cytokines during CPB; (3) IL-10 levels are correlated with the duration of CPB and the liver is a major source of IL-10 during CPB; and (4) steroid pretreatment is an effective intervention to inhibit the release of proinflammatory cytokines and enhance IL-10 production.

Conclusions. The improved knowledge of cytokine responses to CPB may help to develop interventions aimed at reducing postoperative morbidity and mortality.

(Ann Thorac Surg 1997;63:269–76)

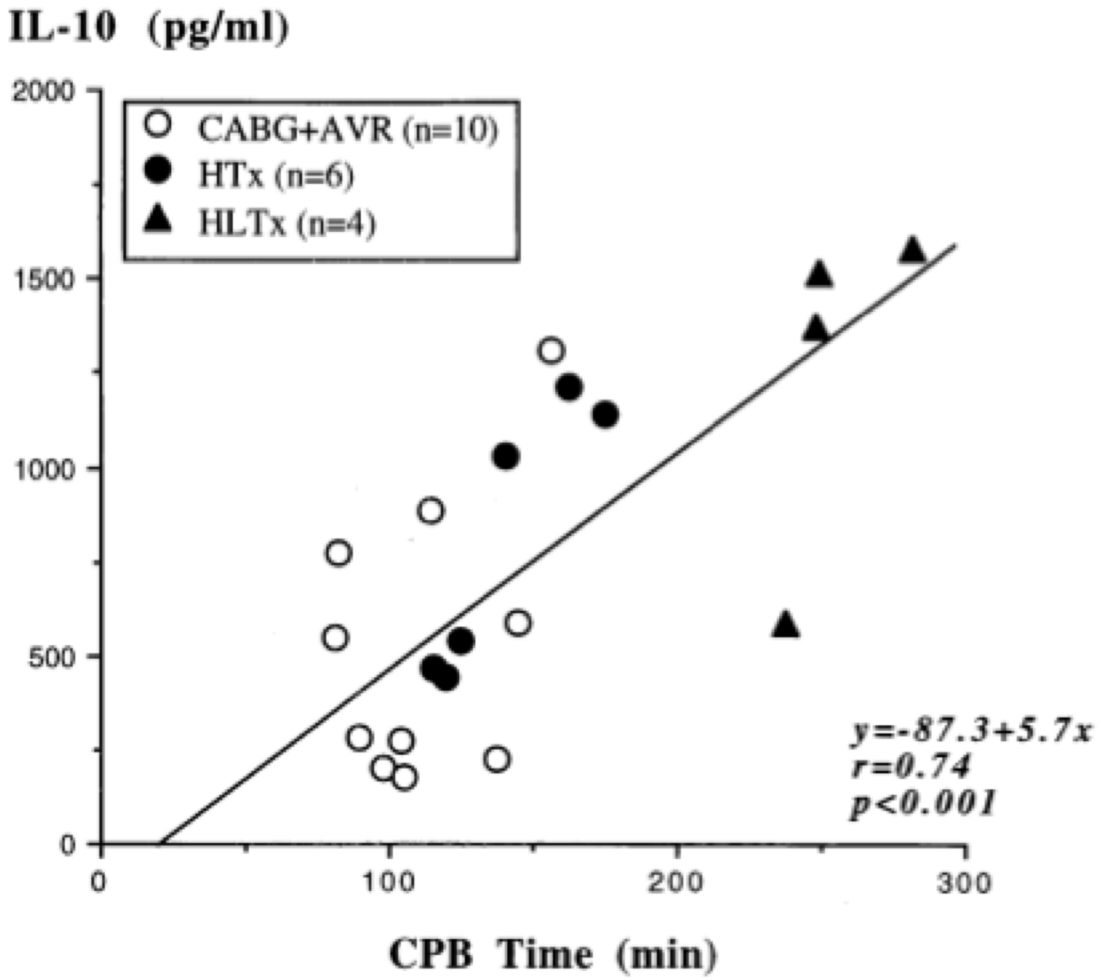

Fig 3. Correlation between arterial interleukin-10 (IL-10) levels and the duration of cardiopulmonary bypass (CPB) 1 hour after aortic declamping in steroid-pretreated patients undergoing routine cardiac operations (coronary artery bypass grafting and aortic valve replacement [CABG+AVR]), heart transplantation (HTx), and heart-lung transplantation (HLTx).

degree of myocardial injury after CPB. A number of anticytokine strategies, including procedures such as hemofiltration, heparin coating of the CPB circuits, or pharmacologic interventions, may be considered to reduce morbidity after CPB. Among these, steroid administration before both hypothermic or normothermic CPB may be a simple, safe, and effective intervention to influence the cytokine responses in open heart operations, not only by inhibiting proinflammatory cytokines TNF-α and IL-8, but also by enhancing the release of antiinflammatory cytokine IL-10. A better understanding

Heparin-Coated Circuits Reduce Myocardial Injury in Heart or Heart-Lung Transplantation: A Prospective, Randomized Study

Song Wan, MD, PhD, Jean-Louis LeClerc, MD, Martine Antoine, MD, Jean-Marie DeSmet, MD, Anthony P. C. Yim, MD, and Jean-Louis Vincent, MD, PhD

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(Ann Thorac Surg 1999;68:1230–5)

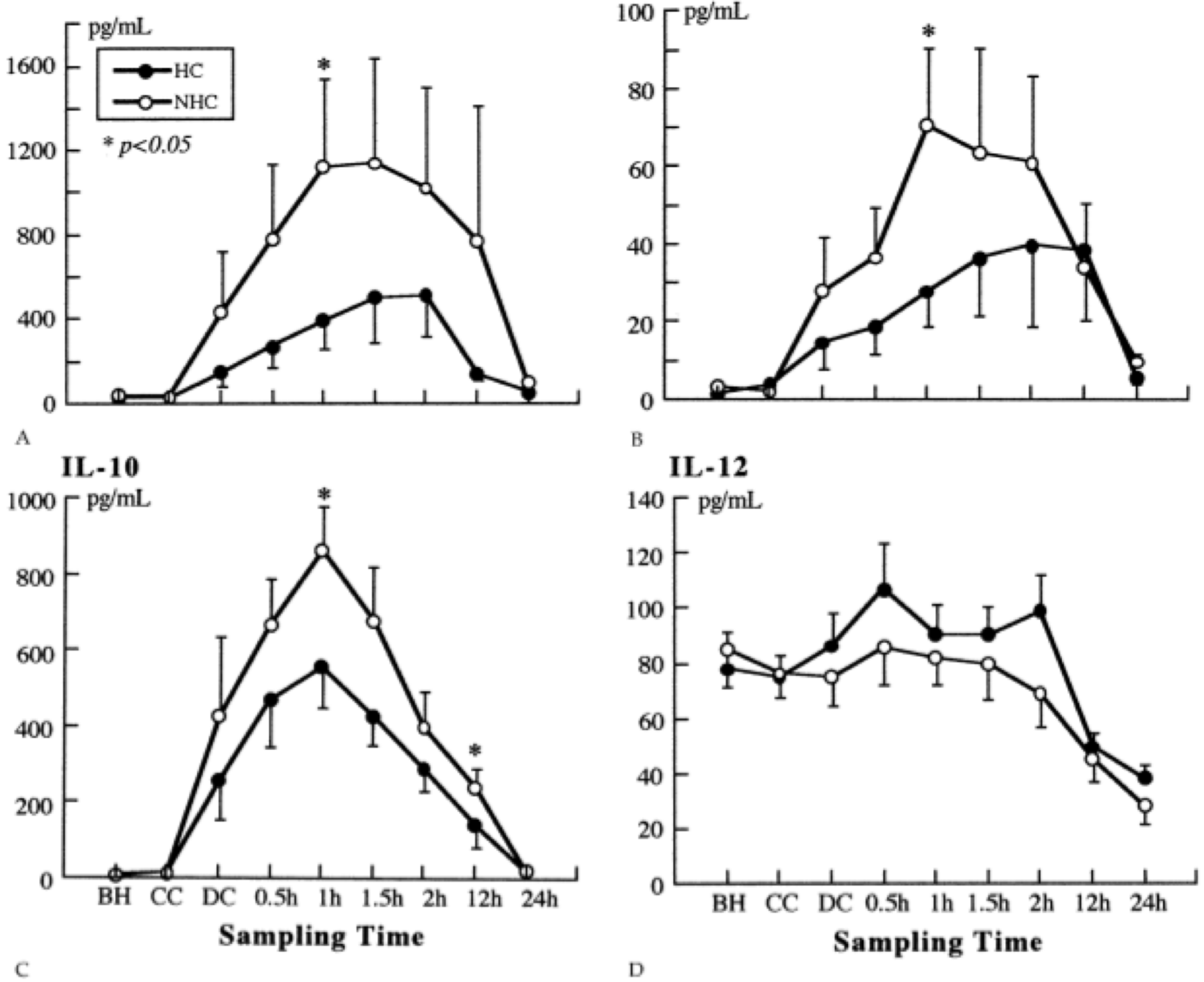

Fig 2. Plasma levels of interleukin (IL)-6 (A), IL-8 (B), IL-10 (C) and IL-12 (D) in patients undergoing heart and heart-lung transplantation with heparin-coated (HC) or noncoated (NHC) extracorporeal circuits. (Sampling time points: see legend of Fig 1.)

Our data indicated that the use of HC circuits with full systemic heparinization is safe in patients suffering from prolonged duration of CPB and ischemia. By limiting both pro- and anti-inflammatory reactions under these conditions, HC circuit may contribute significantly to the reduction in myocardial ischemia-reperfusion injury as suggested by a lower cTnI release following CPB.

There is ground for development

Outline

1. The History
2. The Evidence over Time
3. **The Technical Aspects**
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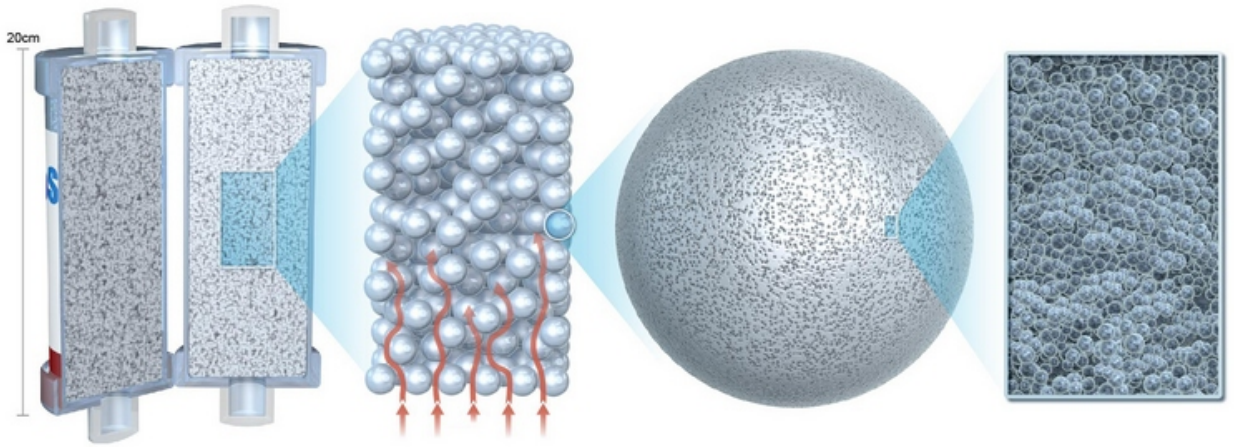
The CytoSorb Adsorber

* Highly biocompatible, porous polymer beads
*Removal of hydrophobic substances due to physicochemical properties
* Pore size



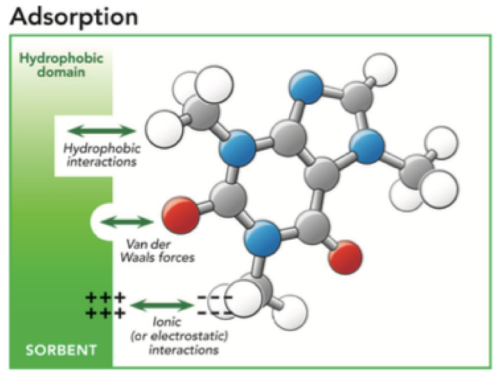


Fig. 3. Adsorption corresponds to the saturable fixation of some molecules directly on a sorbent or a membrane along an affinity gradient depending on ionic, hydrophobic, and van der Waals interactions.

* Substances up to 55kD

The Surface Defines the Performance

Blood contact surface the difference

Bio- and Hemocompatibility

* CytoSorb meets the ISO 10993 standard, that also applies e.g. to implantable devices
* No activation of Coagulation and Complement System
* No removal of:
    - Immunoglobulins
    - Coagulation factors
    - Fibrinogen (340 KD)
    - Coagulation inhibitors AT III / Protein C (65 KD / 62 KD)
* No significant loss of albumin (64 KD)
* Low platelet loss
* Concentration-dependent removal rate of substances (auto-regulation)

Which substances are removed?

Inflammatory mediators

Cytokines (IL-10, IL-6, IL-8, TNF-alpha…)
- Small glycoproteins, 8-40 kDa
- Signal molecules for inter-cellular communication
- Regulators of the immune system and inflammation

„Trigger“ of the inflammatory reaction
- DAMPs (Damage associated molecular patterns)
- PAMPs (Pathogen associated molecular patterns)

Toxines (Enterotoxine)
- Bacterial toxines can also induce cellular damage/death, tissue injury and organ failure
- *S. aureus* toxins
- *S. pyogenes* toxins

Elimination of other harmful substances

Metabolites

* Bilirubin (Hemolysis or liver dysfunction)

* Myoglobin (AKI)

* Free hemoglobin (AKI)

* Ammonia (Contributing to hepatic encephalopathy)

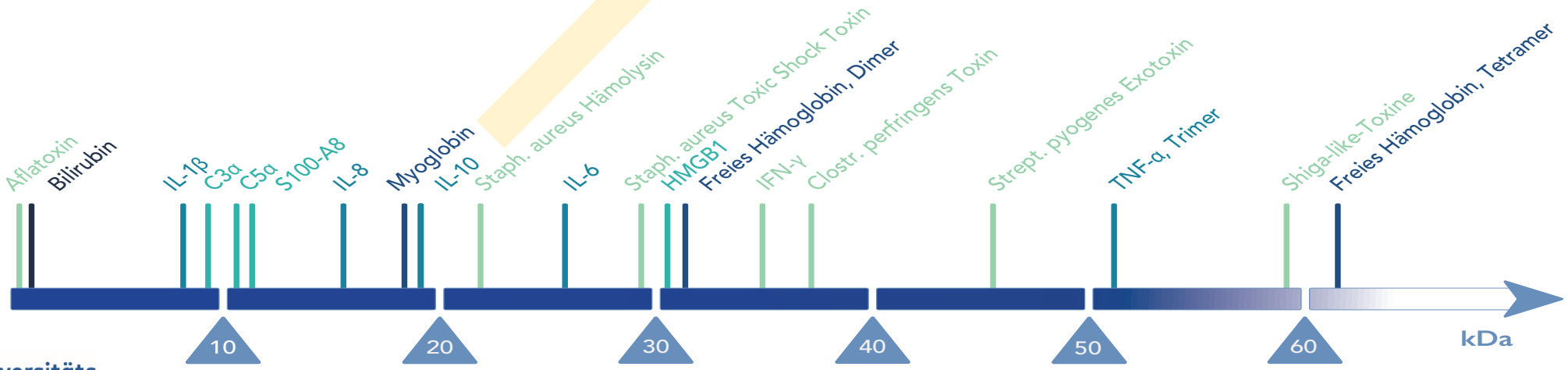
Elimination

* Cytokines (IL-10, IL-6, TNFα)
* Myoglobin
* Bilirubin
* Toxins
* ……

No elimination

* Immunoglobin
* Coagulation factors
* Fibrinogen (340kD)
* AT III / Prot. C (65 / 62kD)
* Albumin (64kD)

…



Indication – Cytosorb - USZ

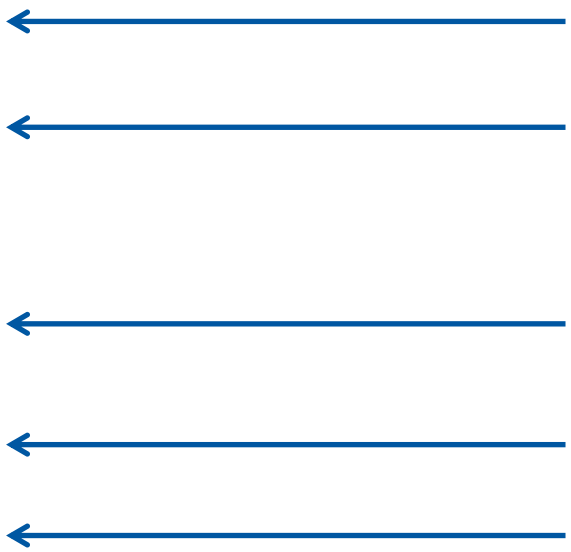
Courtesy of Maximilian Halbe CCP – Chief Perfusionist - USZ

Indication – Cytosorb - USZ

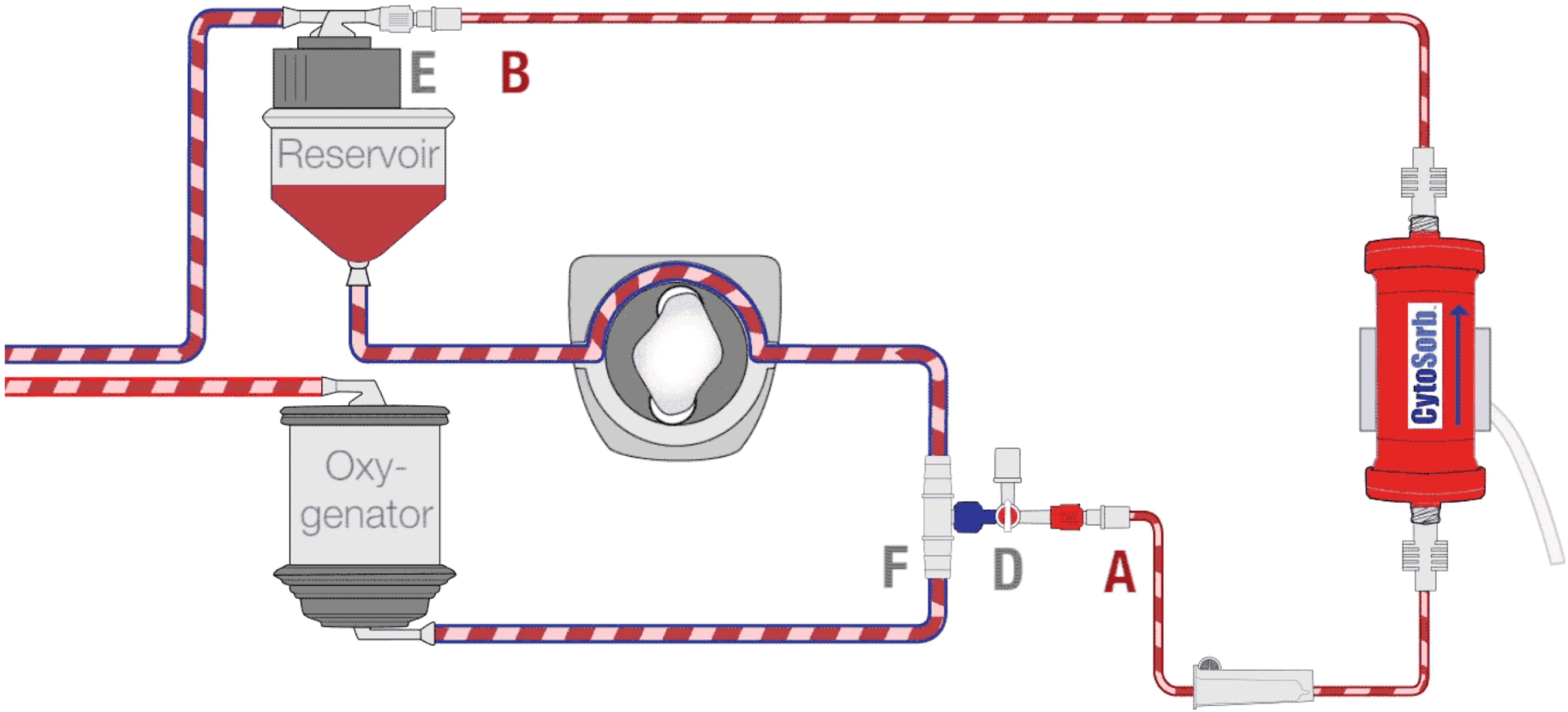
* Extracorporeal Circulation
* ECMO / ECLS
* Additional to Hemofiltration

Indication for Cytosorb ECC - USZ

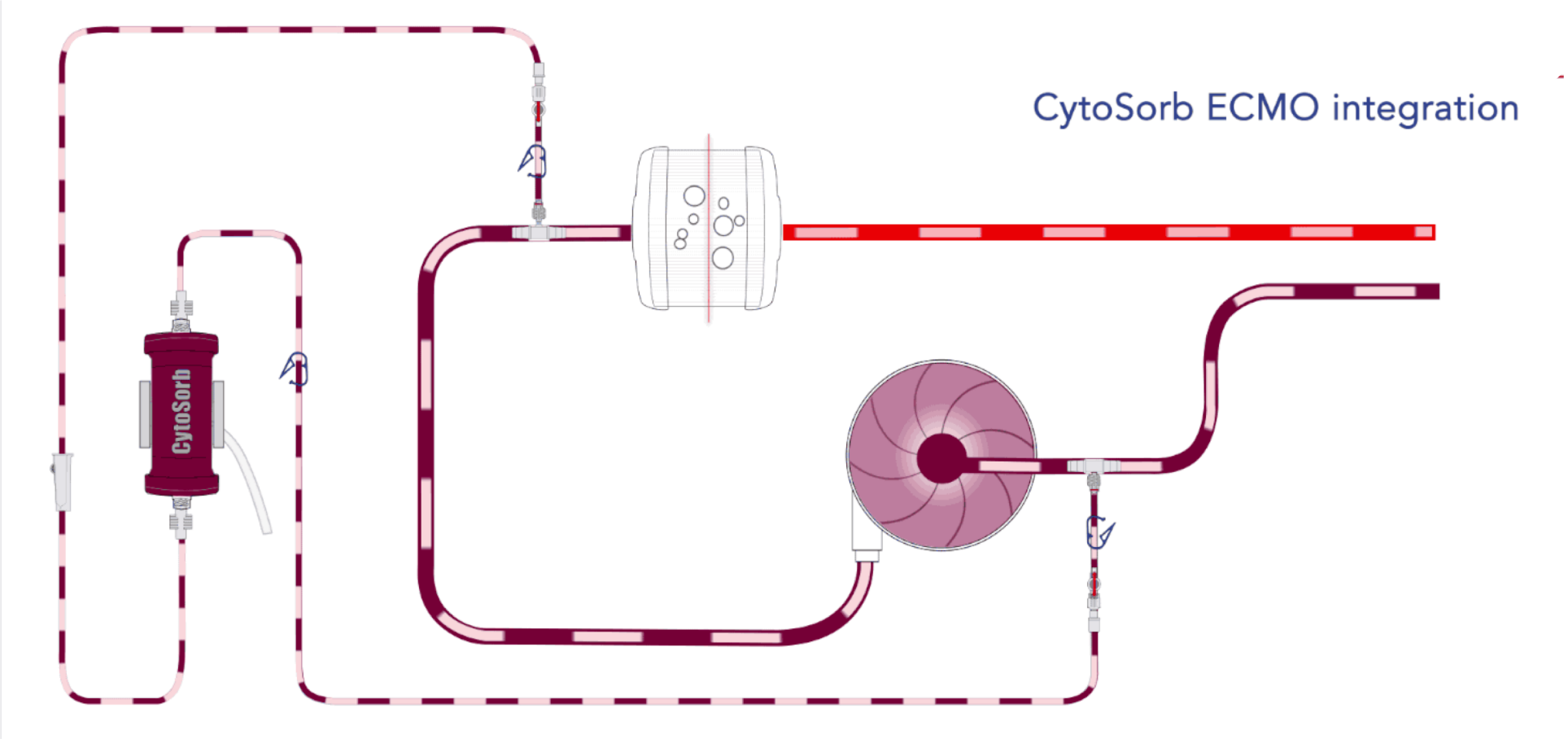
* Sepsis
* Endocarditis
* VAD implantation
* Transplantation
* Long operation expected
* Type A – Dissection
* PTE - PAH



Set-up of CytoSorb - CPB



Set-up of CytoSorb - CPB



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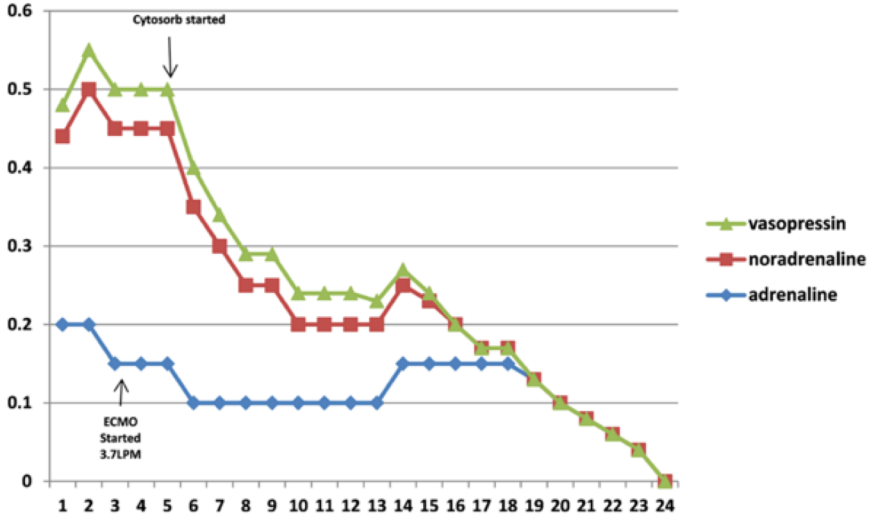
CytoSorb and ECMO

Combination of ECMO and cytokine adsorption therapy for severe sepsis with cardiogenic shock and ARDS due to Panton–Valentine leukocidin—positive *Staphylococcus aureus* pneumonia and H1N1

NJ Lees[1] · AJP Rosenberg[1] · AI Hurtado-Doce[1] · J Jones[1] · N Marczin[3,4,5] · M Zeriouh[2] · A Weymann[2] · A Sabashnikov[2] · AR Simon[2] · AF Popov[2]

J Artif Organs 2016; 19:399-402.



to full recovery of this patient. However, such rapid resolution of neutropenia, reversal of toxic shock, and rapid weaning off of the high-dose vasopressor infusions are unusual for such severe presentation, and we feel that Cytosorb was a beneficial factor in our combination therapy with ECMO IVIg therapy.

CytoSorb and ECMO

Case Report

Perfusion

Perfusion
1–4

DOI: 10.1177/0267659118777442
journals.sagepub.com/home/prf
SAGE

Continuous cytokine haemoadsorption incorporated into a venoarterial ECMO circuit for the management of postcardiotomy cardiogenic and septic shock – a case report

Endre Nemeth,[1] Szabolcs Szigeti,[1] Tamas Varga,[1]
Laszlo Daroczi,[2] Zoltan Barati,[2] Bela Merkely[2] and Janos Gal[1]

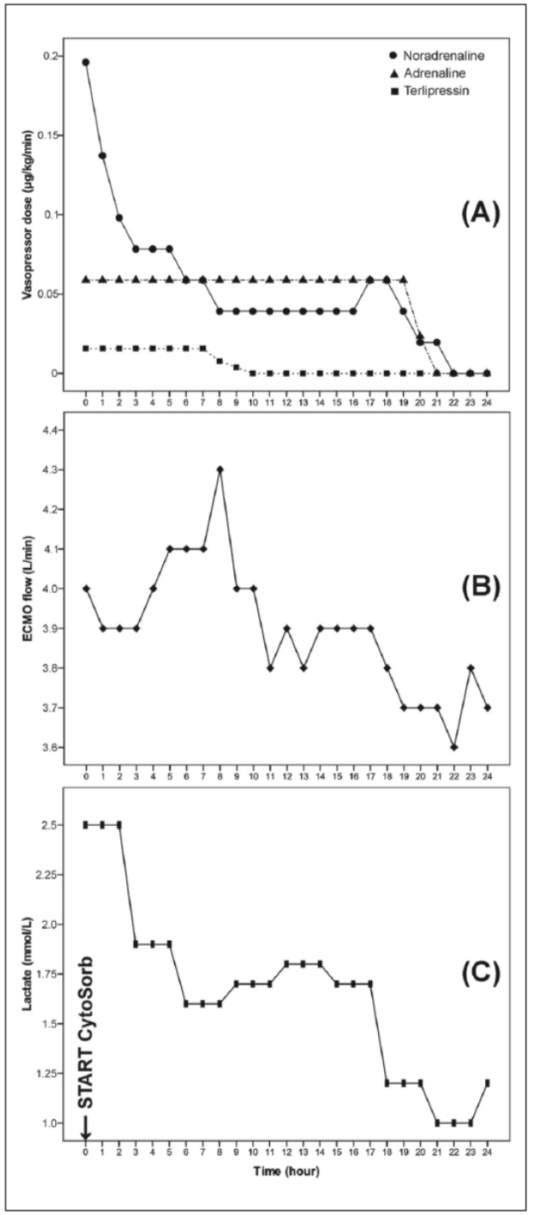


Figure 1. Changes of vasopressors (A), ECMO flow (B) and lactate level (C) during CytoSorb™ treatment used in the venoarterial ECMO circuit. ECMO: extracorporeal membrane oxygenation.

Transplantation

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ORIGINAL PRE-CLINICAL SCIENCE

Cytokine filtration modulates pulmonary metabolism and edema formation during ex vivo lung perfusion

Ilker Iskender, MD, MSc,[a] Tugba Cosgun, MD,[a] Stephan Arni, PhD,[a]
Michael Trinkwitz, MSc,[b] Stefan Fehlings, MSc,[b] Yoshito Yamada, MD, PhD,[a]
Nikola Cesarovic, PhD,[c] Keke Yu, MD,[d] Thomas Frauenfelder, MD,[e]
Wolfgang Jungraithmayr, MD, PhD,[a] Walter Weder, MD,[a] and Ilhan Inci, MD[a]

AATS 2019 #92

CONCLUSIONS: Continuous perfusate filtration through sorbent beads is effective and safe during prolonged EVLP. Cytokine removal decreased the development of pulmonary edema and electrolyte imbalance through the suppression of anaerobic glycolysis and neutrophil activation in this setting.

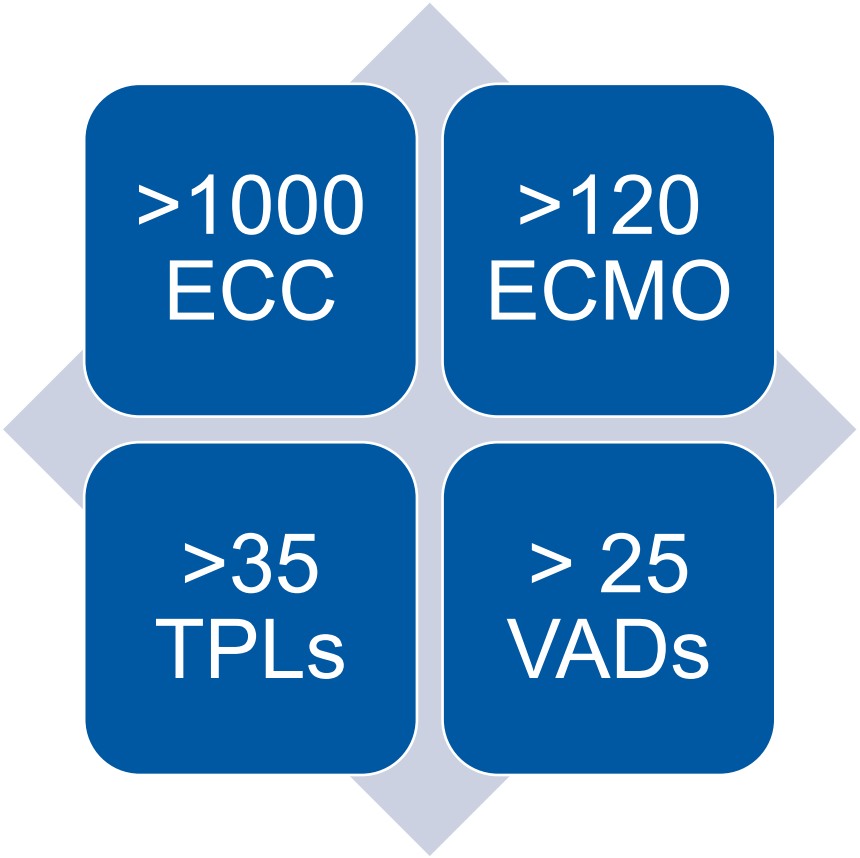
Ongoing Study

USZ - Effect of Cytosorb™ on short-term outcome of patients with Acute Type Aortic Dissection

* Retrospective
* Observational
* Single-center

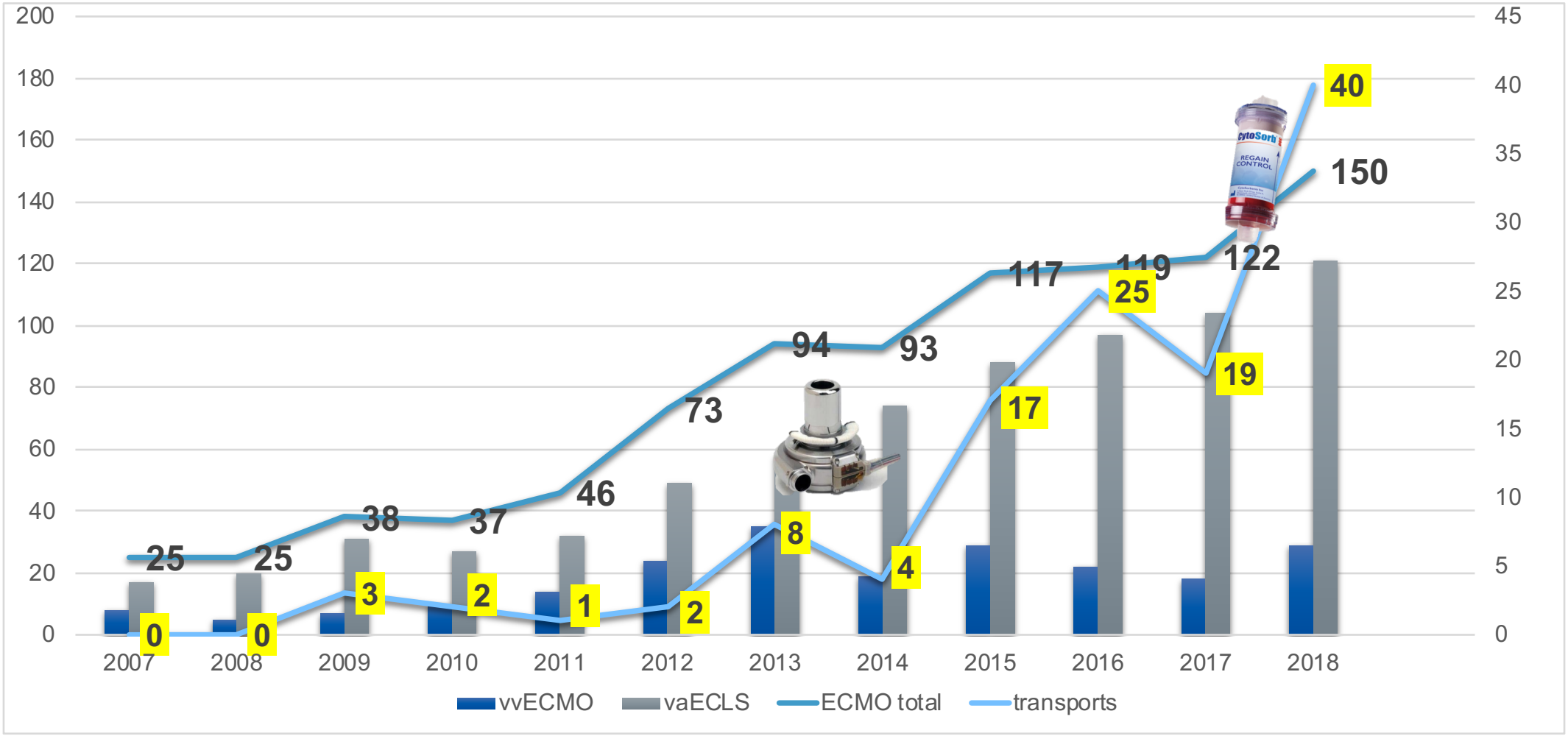
USZ – App 60 patients Acute Type A/year

USZ Activity



02/2015 –
03/2019
>600 Cytosorb
Adsorber

ECMO Programme at USZ



* Aim: effect of hemoadsorption on changes of cytokine levels during CPB > 120 min (CABG, valve surgery)

* Design: RCT, 37 blinded patients (HA 19, control 18)

* Primary outcome was differences of cytokine levels (IL-1β, IL-6, IL-18, TNF-α, and IL-10) within the first five postoperative days

Crit Care. 2016; 20:96

Results

* No removal of albumin
* No serious adverse events
* 80% lower expression of PCT
* No influence on perioperative course
* Inhomogenous / interindividual cytokine activation during CPB
* After HA long lasting effect on IL-10

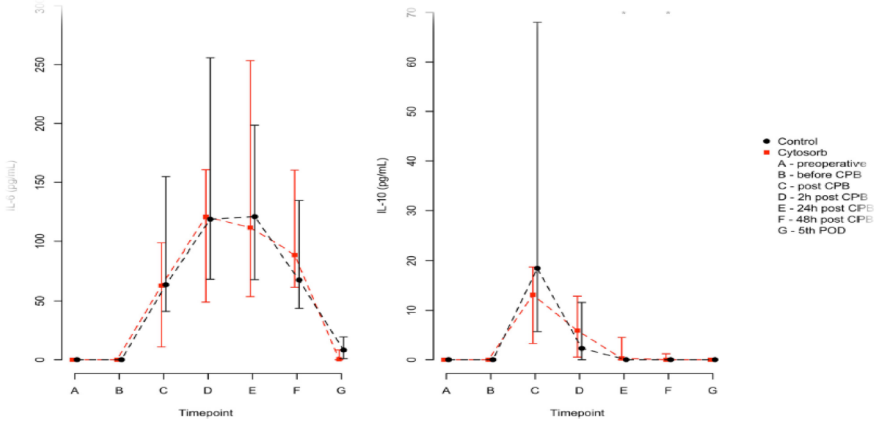
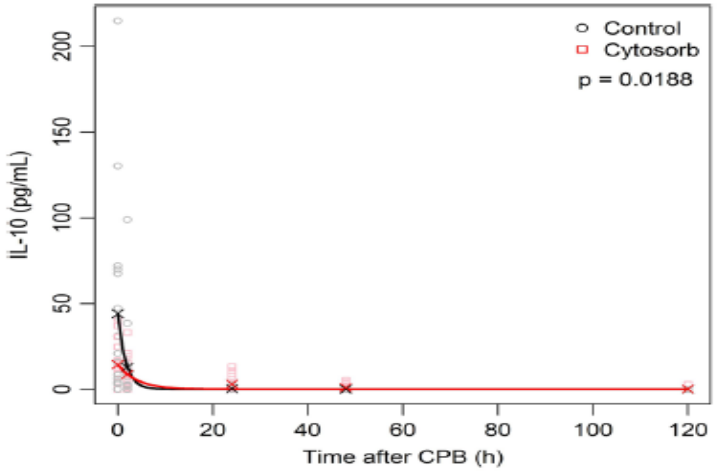


Fig. 2 Comparison of median cytokine levels in picograms per milliliter. Red lines indicate the patients in the CytoSorb™ treatment group. Black lines indicate the patients in the control group. Error bars correspond to interquartile ranges (first quartile, third quartile). Asterisks mark



Crit Care. 2016;20:96.

*** Infective endocarditis (IE) is associated with high hospital mortality & morbidity**

*** Possible circulatory failure in patients who undergo cardiac surgery for IE**

*** Release of vaso-dilatatory mediators and cytokines**

*** Elimination may improve surgical outcomes by reducing inflammatory response**

Kühne LU, Binczyk R, Riess FC

Comparison of intraoperative vs intraoperative plus postoperative hemoadsorption therapy in cardiac surgery patients with endocarditis

Int J Artif Organs 2019 Feb 25:391398819831301 doi: 10.1177/391398819831301

N = 20

*** Stabilization of hemodynamics and inflammatory parameters in both groups**

*** Postoperative continuation could be beneficial (24-48h)**

Hemoadsorption treatment of patients with acute infective endocarditis during surgery with cardiopulmonary bypass - a case series

Karl Träger[1], Christian Skrabal[2], Guenther Fischer[1], Thomas Datzmann[1], Janpeter Schroeder[1], Daniel Fritzler[1], Jan Hartmann[1], Andreas Liebold[2], Helmut Reinelt[1]

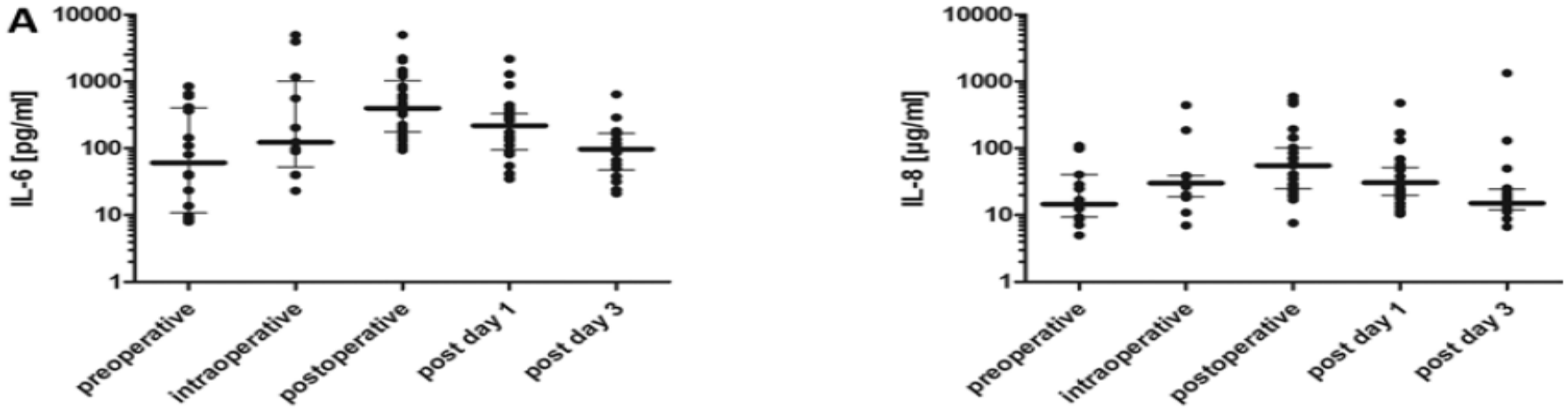
*** 39 patients with proven IE undergoing valve replacement with CytoSorb (HA) compared to a historical group of 28 patients without intraoperative hemoadsorption**

*** All types of endocarditis (AV, MV, TV) included**

Int J Artif Organs 2017; 40:240-49

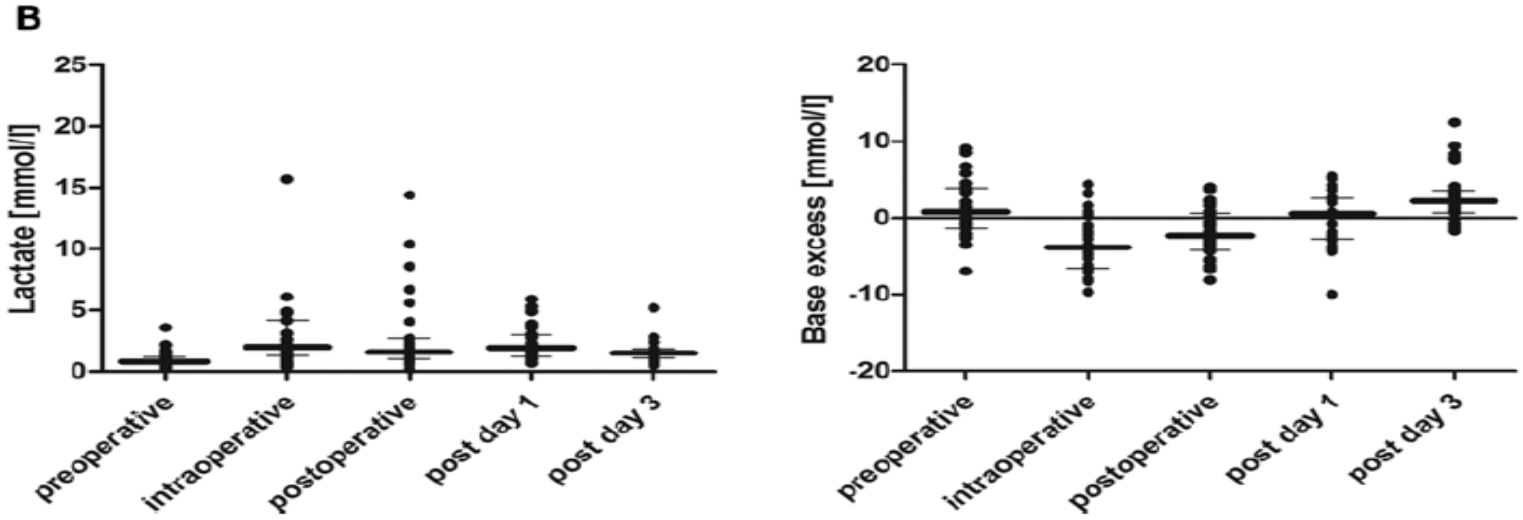
HA group

Course of IL-6 and IL-8



Course of Lactate & BE

Course of Lactate & BE
Historical control



Int J Artif Organs 2017;40:240-49

Clinical effects of intraoperative hemoadsorption in acute infective endocarditis patients

DGHGC 2019

Courtesy of Prof. D. Wendt

- **Effect of intraoperative hemoadsorption in patients with *native isolated mitral valve infective endocarditis***

- **Between January 2014 und July 2018, 58 consecutive patients**

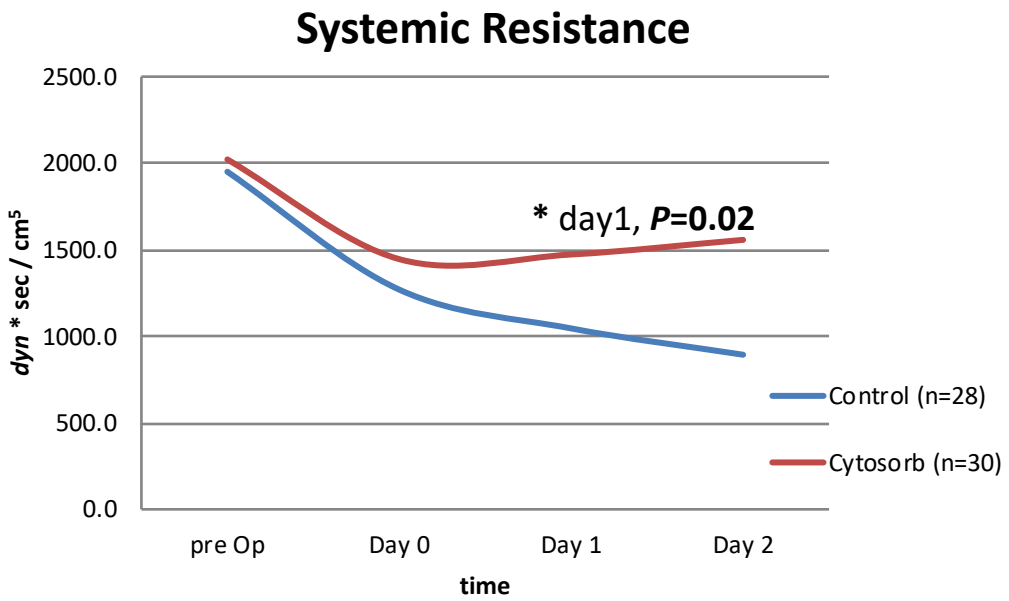
Group A	**N=30**	**Intraoperative hemoadsorption (HA)**
Group B	**N=28**	**No hemoadsorption was used**

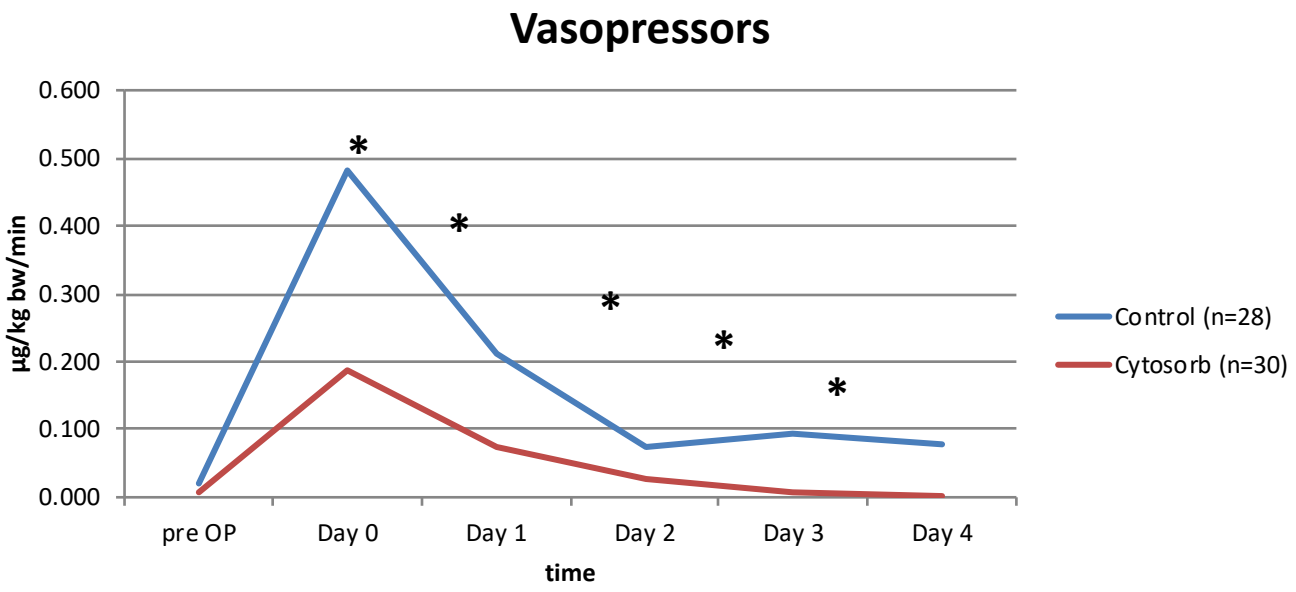
- **Primary endpoint: occurrence of postoperative sepsis as defined by The Third International Consensus Definitions for Sepsis and Septic Shock and sepsis-related death (SEPSIS-3)[1]**

- **Secondary endpoints: overall in-hospital mortality, need for postoperative vasopressors and ICU-stay**

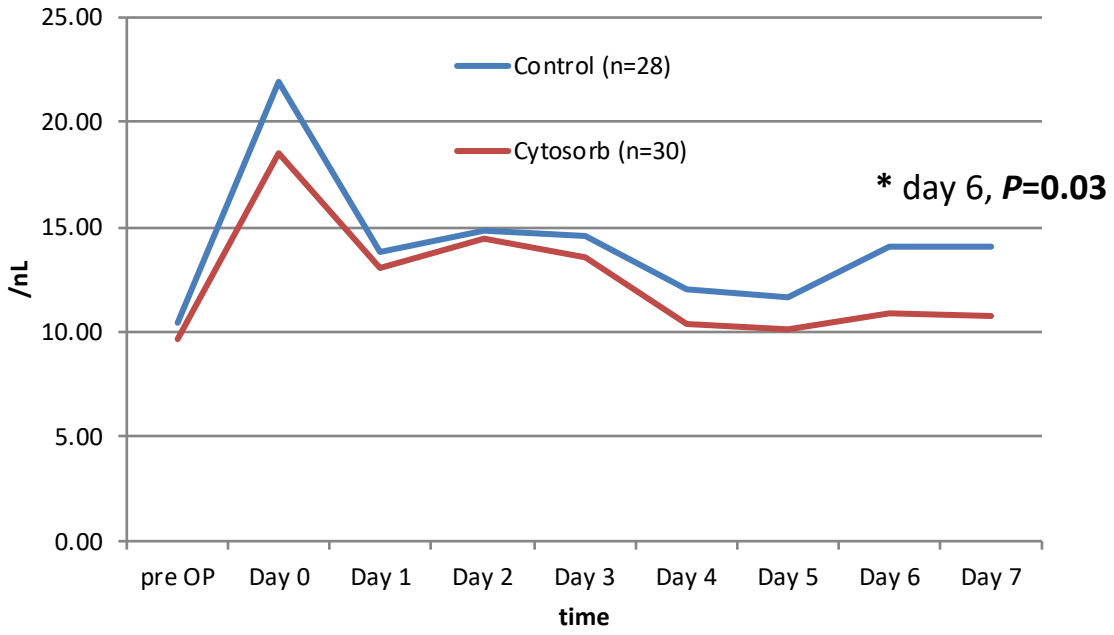
	All patients N=58	With HA N=30	Without HA N=28	*P-Value*
Clinical status				
NYHA* III-IV	31 (53.4)	15 (50.0)	16 (57.1)	0.586
Preoperative intubated	9 (15.5)	5 (16.7)	4 (14.3)	0.802
Preoperative vasopressor	7 (12.1)	3 (10.0)	4 (14.3)	0.617
Identified pathogens				
Staphylococcus species	20 (34.4)	14 (46.7)	6 (21.4)	0.043
Staphylococcus aureus	**15**	**10**	**5**	**0.205**
MSSA	14/15	9/10	5/5	0.280
MRSA	1/15	1/10	-	0.330
Streptococcus species	11 (19.0)	8 (26.6)	3 (10.7)	0.121
Enterococcus species	4 (6.9)	-	4 (14.3)	0.032
Other	6 (10.3)	3 (10.0)	3 (10.7)	0.929
Negative culture	**17**	**5**	**12**	**0.029**
Good LVF (LVEF >50%)	48 (82.8)	24 (80.0)	24 (85.7)	0.565
Poor LVF (LVEF <35%)	1 (1.7)	-	1 (3.6)	0.296
Severe mitral regurgitation	40 (69.0)	19 (63.3)	21 (75.0)	0.337
Concomitant aortic/tricuspid valve disease	14 (24.1)	5 (16.7)	9 (32.1)	0.169

	All patients N=58	With HA N=30	Without HA N=28	*P-value*
Days between diagnosis and surgery	9 (3-21)	12 (6-22)	6 (1-20)	0.064
Indication for surgery				
Large/embolic vegetation	**35**	**23**	**12**	**0.009**
Heart failure	**14**	**3**	**11**	**0.009**
Severe mitral regurgitation	6 (10.3)	4 (13.3)	2 (7.1)	0.439
Sepsis	3 (5.2)	-	3 (10.7)	0.066
Isolated mitral valve surgery	30 (51.7)	18 (60.0)	12 (42.9)	0.192
Mitral valve repair	**35**	**23**	**12**	**0.009**
Mitral valve replacement	**23**	**7**	**16**	**0.009**
Concomitant AV/TV procedure	14 (24.1)	5 (16.7)	9 (32.1)	0.169
CPB time, minutes	101 (76-127)	85 (74-106)	116 (79-149)	0.115
ACC time, minutes	61 (46-83)	59 (45-78)	74 (49-106)	0.067

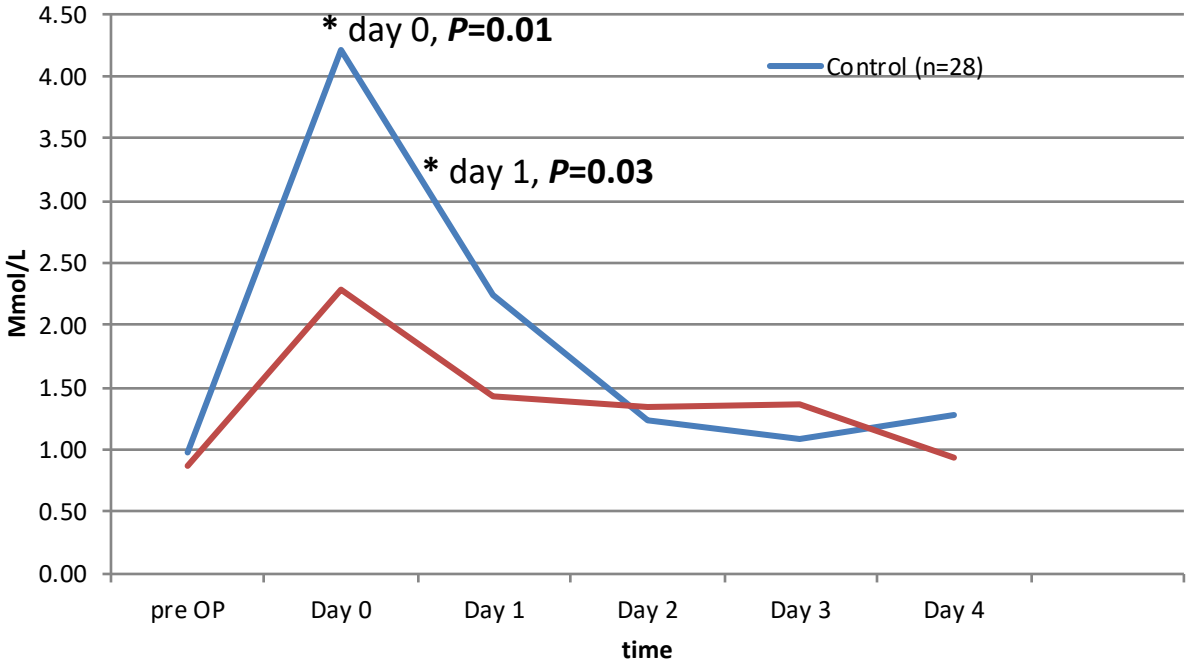

Systemic Resistance
2500.0
2000.0
1500.0
1000.0
500.0
0.0
dyn * sec / cm5
* day1, P=0.02
Control (n=28)
Cytosorb (n=30)
pre Op
Day 0
Day 1
Day 2
time

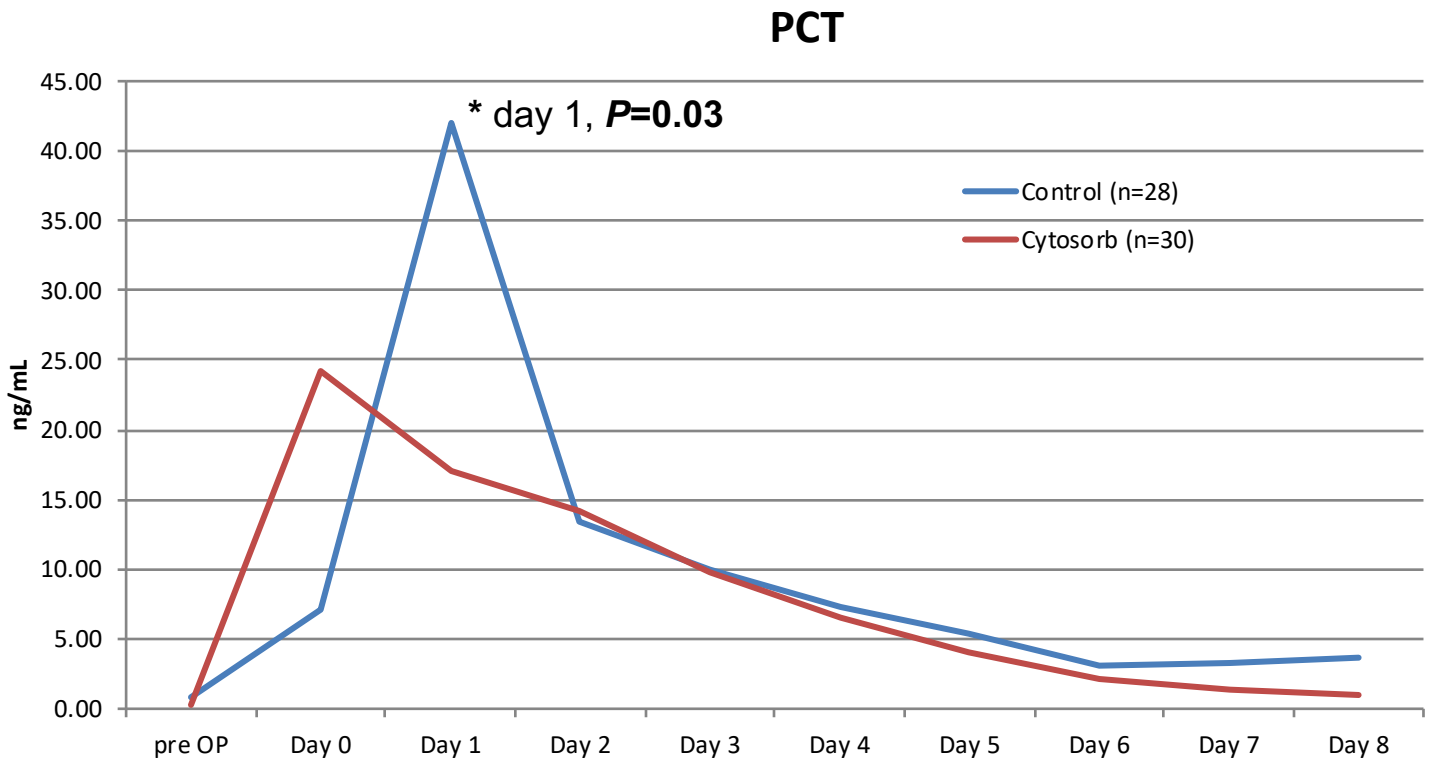

Vasopressors
0.600
0.500
0.400
0.300
0.200
0.100
0.000
µg/kg bw/min
*
*
*
*
*
Control (n=28)
Cytosorb (n=30)
pre OP
Day 0
Day 1
Day 2
Day 3
Day 4
time

leucocytes



lactate




PCT
* day 1, P=0.03
Control (n=28)
Cytosorb (n=30)
ng/mL
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
pre OP
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8

	With HA N=30	Without HA N=28	P-Value
Primary			
Sepsis	**5**	**11**	**0.054**
Sepsis-related death	**-**	**4**	**0.032**
Secondary			
In-hospital mortality	3 (10.0)	5 (17.9)	0.386
Vasopressor at ICU-arrival	**0.19**	**0.48**	**0.069**
ICU-stay, days	3 (2-10)	3 (2-11)	0.771

REMOVE study (NCT03266302)

Revealing mechanisms and investigating efficacy of hemoadsorption for prevention of vasodilatory shock in cardiac surgery patients with infective endocarditis – a multicentric randomized controlled trial

January 17, 2018, estimated primary completion date December 2019

REMOVE study (NCT03266302)

- **Primary endpoint: SOFA Score** ***(Sepsis-related organ failure assessment score)***

- **Secondary endpoints:**
  - **Overall mortality**
  - **Changes in cytokine and cfDNA levels (only for the first 2x25 pts.)**
  - **SOFA subscores**
  - **Days on ventilator, vasopressor and renal replacement therapy**
  - **incidence of stroke**
  - **length of ICU and in-hospital stay**

Outline

1. The History
2. The Evidence over Time
3. The Technical Aspects
4. Current Knowledge
5. **Conclusions**

We have different tools to address old needs

* Small retrospective and CRs

* First beneficial hints in endocarditis

* Easy to use, no device-related SAEs (>600)

* Further investigation / larger RCTs needed

In patients with a high level of a systemic inflammation:

1. Hemoadsorption may enhance intra- and postoperative hemodynamic stability
2. Reduction in postoperative vasopressor requirements

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