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HEMOADSORPTION IMPROVES INTRAOPERATIVE HEMODYNAMICS AND METABOLICS DURING AORTIC ARCH SURGERY REQUIRING HYPOTHERMIC CIRCULATORY ARREST

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Disclosure

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I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

- ■ I do not have any potential conflict of interest

Background

- Systemic inflammatory response syndrome (SIRS) is common after cardiovascular surgery using cardiopulmonary bypass (CPB)

→ Vasoplegia, organ dysfunction, death[1]

- Aortic surgery extending into the aortic arch requires mild to deep hypothermia and circulatory arrest (HCA) with adjunct selective antegrade cerebral perfusion (SACP)

→ 2nd inflammatory trigger[2]

- Hemoadsorption (HA) may potentially alleviate inflammatory response associated with HCA[3]

→ Rapid elimination of proinflammatory cytokines from the blood (sepsis studies)

[1]Stoppelkamp S *PLoS* 2015
[2]Luehr M Eur *J Cardiothor Surg* 2014
[3]Trager K *Int J Artif Organs* 2016

Pilot studies on HA in cardiovascular surgery

- Pilot study on the effects of HA in cardiac surgery (n=37)[1]
  - No effects of HA on need for vasopressors
  - No effects of HA on need for blood transfusion
  - No effects of HA on mortality
  - HA during CPB is feasible and safe → **benefit for patients with SIRS?**

- Pilot study on the effects of HA in cardiac transplantation (n=32)[2]
  - Need for vasopressors↓
  - Need for RRT↓
  - Trend towards shorter length of MV and ICU stay
  - **HA treatment without obvious adverse events → benefit for patients with ischemia/reperfusion?**

[1]Bernardi MH *Crit Care* 2016
[2]Nemeth E *Clin Transplant* 2018

Study objective

→ Elucidate effects of HA on

- Intraoperative hemodynamics,
- Intraoperative metabolics,
- Intraoperative need for blood transfusion,
- Intraoperative regional cerebral SO_2 (cSO_2) using cerebral near-infrared spectroscopy (NIRS),

Assessment of cSO_2 using NIRS monitoring in (cardiac) surgery

- Effects of active NIRS monitoring on perioperative mortality uncertain in general surgery[1]
  - Systematic review, 15 studies, 1822 adult participants
- Impairment of intraoperative cerebral blood flow autoregulation (including NIRS monitoring) is not predictive of early POCD in elderly patients in non-cardiac surgery [2]
  - Prospective study, 82 patients
- NIRS monitoring is feasible and safe

- Reductions in regional cSO_2 during cardiac surgery may identify CPB cannula malposition (particularly in aortic surgery)[3]
  - Systematic review, 13 case reports, 28 observational studies, 2 RCTs
- (Preoperative) regional $cSO_2\downarrow \rightarrow$ postoperative neurologic complications? (low level evidence)
- Regional $cSO_2\uparrow \rightarrow$ prevention of stroke/POCD? (insufficient data)

[1]Yu Y *Cochrane Database Syst Rev* 2018
[2]Goettel N *Anesth Analg* 2017
[2]Zheng F *Anesth Analg* 2013

Study objective

→ Elucidate effects of HA on

- Intraoperative hemodynamics,
- Intraoperative metabolics,
- Intraoperative need for blood transfusion,
- Intraoperative regional cerebral SO_2 (cSO_2) using cerebral near-infrared spectroscopy (NIRS),
- Postoperative outcome

in patients undergoing aortic arch surgery with HCA

→ ischemia/reperfusion injury

→ possible SIRS

→ potential benefit for HA?

Patients / Methods

- Retrospective study at a single German aortic center (2013-2017)
- 780 consecutive patients undergoing aortic surgery with HCA (25-26°C) with adjunct SACP (22°C, 50-60 mmHg pressure control)[1]
- Propensity score matching (nearest neighbor, caliper 0.2) unaware of outcome parameters

  → 176 with HA (CytoSorb®, CytoSorbents GmbH, Berlin, Germany)

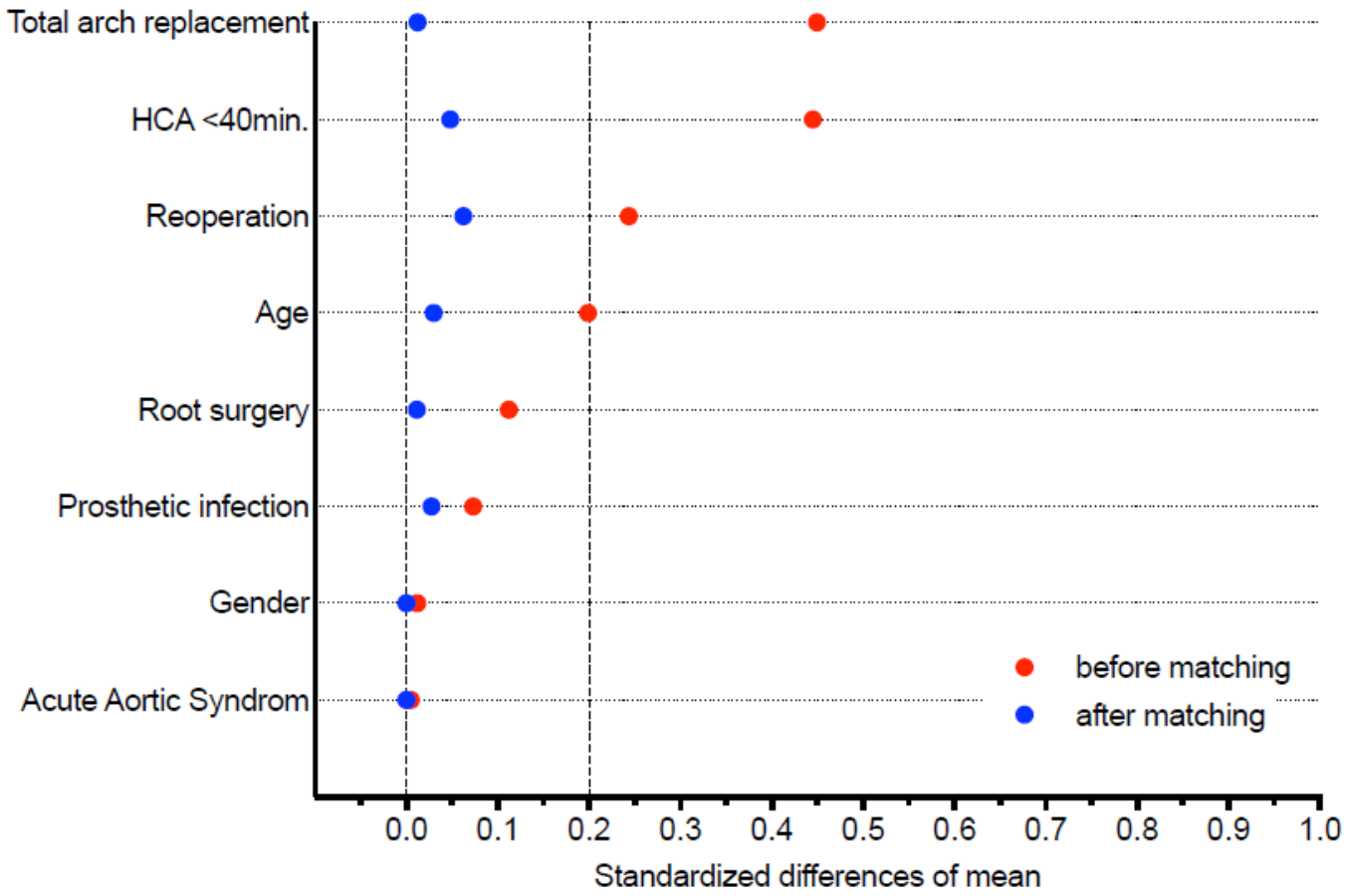
  → 168 pairs (n=336) matched with propensity score (Control/HA)
  - Subgroup: elective surgery of aortic aneurysm (87 with matching partners)
  - Subgroup: acute aortic syndrome (46 with matching partners)

- Student‘s t-test (mean±SD) or Mann-Whitney U (median, 25%/75% percentiles)
- Chi-square test or Fisher‘s exact test
- α error of 5% ($p<0.05$)

[1]Peterss S *Eur J Cardiothor Surg* 2017

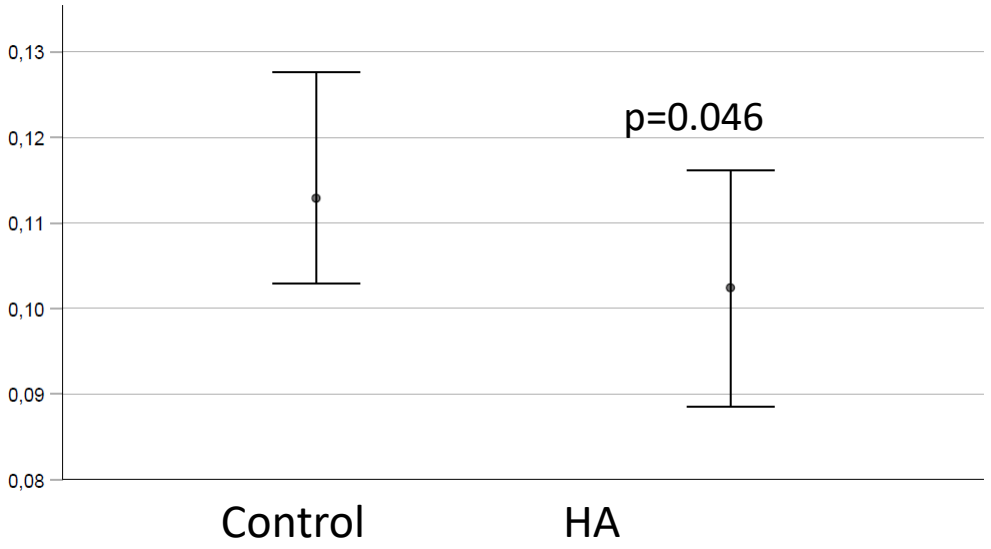
Propensity score matching

Total cohort



Intraoperative need for vasopressors

Total cohort: norepinephrine [µg/kg/min]



n=336

epinephrine (µg/kg/min)	0.016 (0.008–0.028)	0.013 (0.005–0.025)	0.126
postoperative use of vasopressin	35 (10.4%)	30 (8.9%)	0.581
vasopressin dose since end of CPB (IE/h)	2.70 (±3.35)	1.44 (±0.83)	0.039
lowest intraoperative pH	7.245 (7.192–7.282)	7.254 (7.208–7.294)	0.083
highest intraoperative lactate (mmol/l)	4.23 (2.95–6.87)	3.75 (2.80–5.60)	0.078
use of trometamol	23 (13.7%)	11 (6.5%)	0.045

Hemodynamic stability

Less metabolic acidosis

Intraoperative transfusion requirements

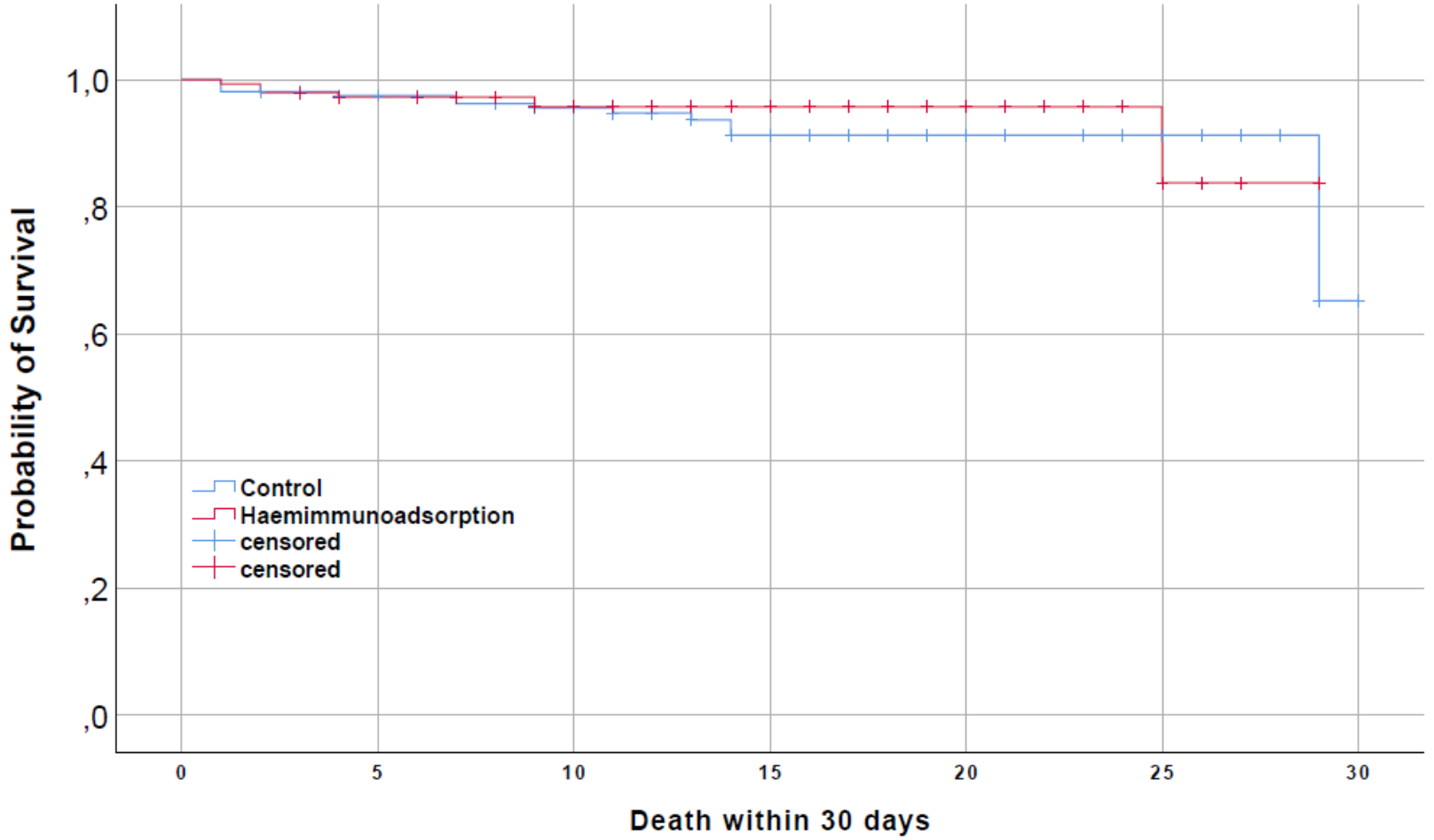
Total cohort

n=336

	Control	HA	p
PRBC (ml)	600 (0–1200)	300 (0–900)	0.0394
	Less blood transfusion		
FFP (ml)	1,500 (750–2250)	750 (750–1500)	0.002
prothrombin complex concentrate (kIE)	4.0 (3.0–6.0)	4.8 (3.6–7.2)	0.0013
fibrinogen (g)	4 (4–8)	4 (4–6)	0.113
additional use of tranexamic acid	55 (32.7%)	26 (15.5%)	0.0003

Perioperative mortality

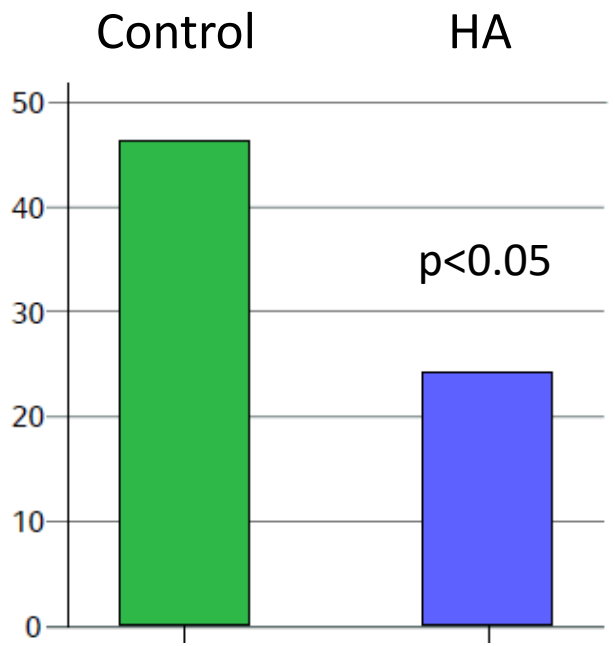
Total cohort



n=336

NIRS incidence

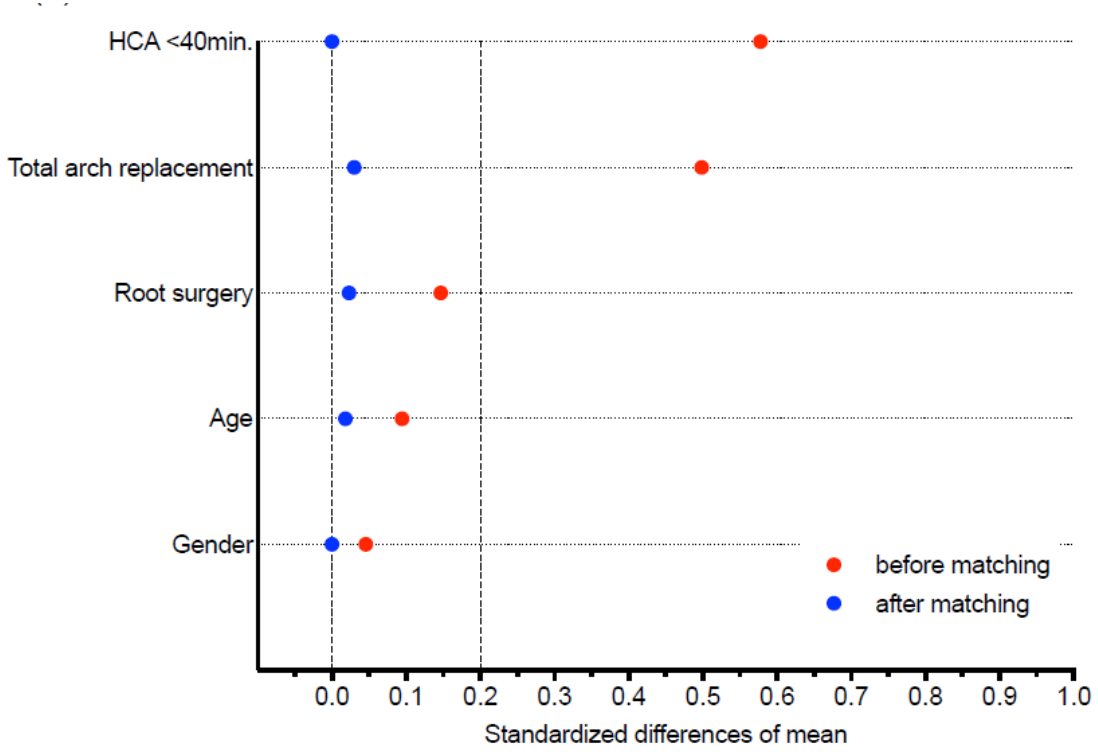
Total cohort: reduction <75% of baseline → yes/no



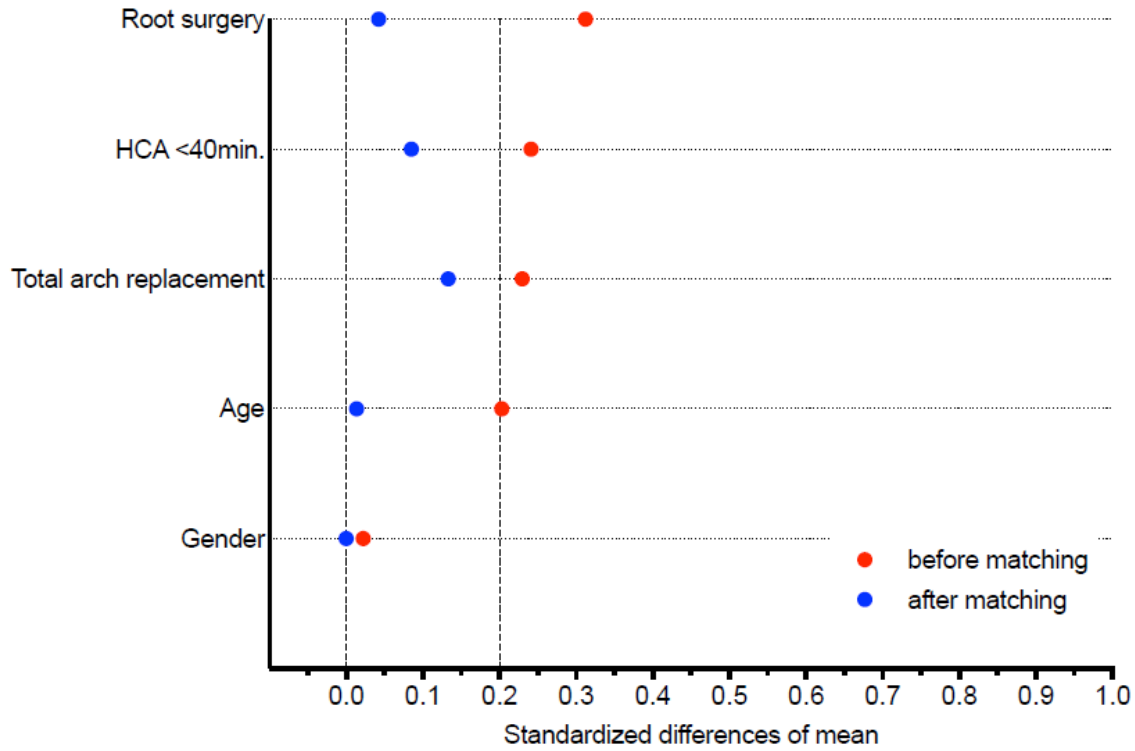
n=336

Subgroup analysis: Propensity score matching

elective aneurysms (n=174)



acute aortic syndrome (n=92)



Subgroup analysis: intraoperative transfusion requirements

- Subgroup: elective surgery of aortic aneurysm (87 with matching partners)

→ no effects of HA

- Subgroup: acute aortic syndrome (46 with matching partners)

	Control	HA	p
PRBC (ml)	1,200 (450–1500)	500 (188–1200)	0.035
	Less blood transfusion		
FFP (ml)	1,500 (750–2250)	1,125 (750–1500)	0.015
prothrombin complex concentrate (kIE)	6.2 (4.1–7.2)	5.9 (4.8–7.2)	0.859
fibrinogen (g)	6.0 (6.0–8.5)	6.0 (4.0–6.0)	0.009

Conclusion / Perspective

- In aortic surgery under HCA with SACP, HA…

… provides hemodynamic stability (need for norepinephrine↓, vasopressin↓)

… attenuates metabolic acidosis (need for trometamol↓)

… reduces blood transfusion (need for packed RBC↓/FFP↓, need for additional tranexamic acid↓)

… increases the use of prothrombin complex concentrate

… may improve cerebral oxygenation (episodes of NIRS <75% of baseline↓)

… provides benefit in the subgroup of patients with acute aortic syndrome (need for packed RBC↓)

… provides no benefit in the subgroup of patients with elective surgery of aortic aneurysm (no SIRS?)

→ HA should be performed in aortic surgery under HCA (especially if prolonged HCA is expected)

→ Effects of HA should be analyzed prospectively in multicenter studies in „inflammatory“ subgroups (endocarditis, reoperations)

Thank you for your attention!

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Supplementals

CytoSorb® adsorption spectrum

Cytokines	MW [kD]	relevant?
IFN-γ	35	Yes
IL-1ß	8	Yes
IL-6	26	Yes
IL-8	17	Yes
IL-10	18	Yes
TNF-α, trimer	51	Yes
PAMPS *(Pathogen Associated Molecular Patterns)*		
Aflatoxin	0.3	Yes
Clostr. perfringens toxin	35	Yes
Shiga-like-toxins	60	Yes
Staph. aureus hemolysin	23	Yes
Staph. aureus toxic shock toxin	29	Yes
Strept. pyogenes exotoxin	46	Yes
DAMPS *(Damage Associated Molecular Patterns)*		
C3a	9	Yes
C5a	11.5	Yes
HMGB-1	30	Yes
PCT	13	Yes
S100	12	Yes
Metabolites		
Ammonia	0.02	Yes
Bile acids	25-67	Yes
Bilirubin	0.6	Yes

Proteins	MW [kD]	relevant?
Albumin	66	No
Antithrombin III	65	Not expected
Myoglobin	17.8	Yes
Protein C	62	Not expected
Immunosuppressants		
Cortisone	0.36	Possible
Coagulation		
Prothrombinase/Tenase complexes	>100	Not expected
Fibrinogen	340	Not expected
Antibiotics**		
Aminoglycosides		Possible
Carbapenems		No
Linezolid		Not expected
Piperacillin/Tazobactam		No
Teicoplanin		Possible
Vancomycin		Yes
Medication		
Amiodarone		No
Digoxin		Yes
Amlodipine		Yes
Verapamil		Yes
Diazepam		Yes
Amitriptyline		Yes
Quetiapin		Yes
Venlafaxine		Yes
Heparin		No
Ticagrelor		Yes
Rivaroxaban		Yes
Dabigatran		Yes