Postoperative hemoadsorption in high-risk cardiac surgery patients – in whom, when and how should we do it?

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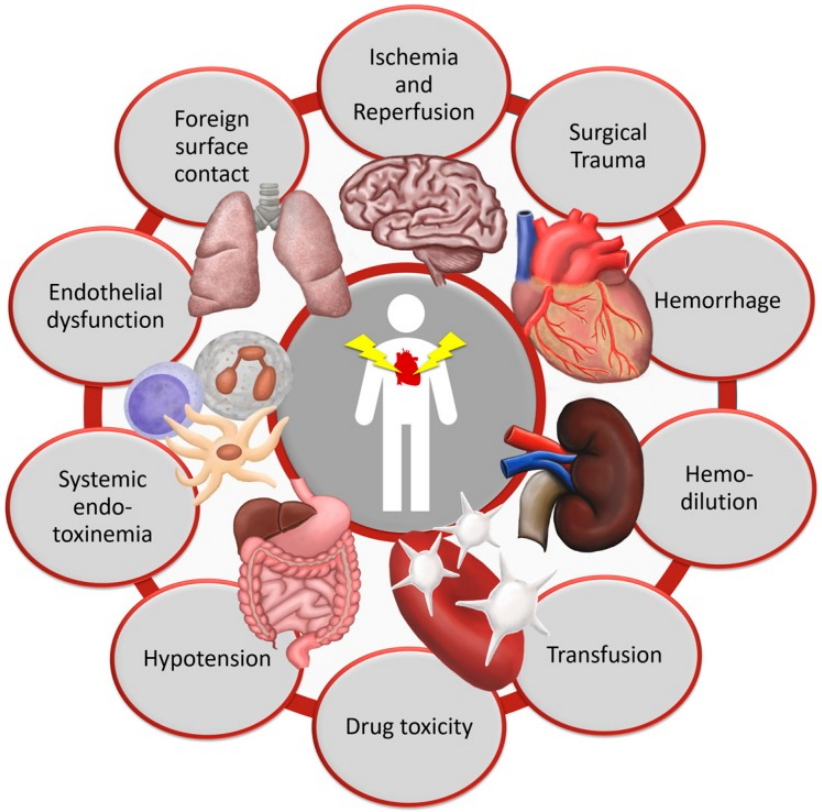
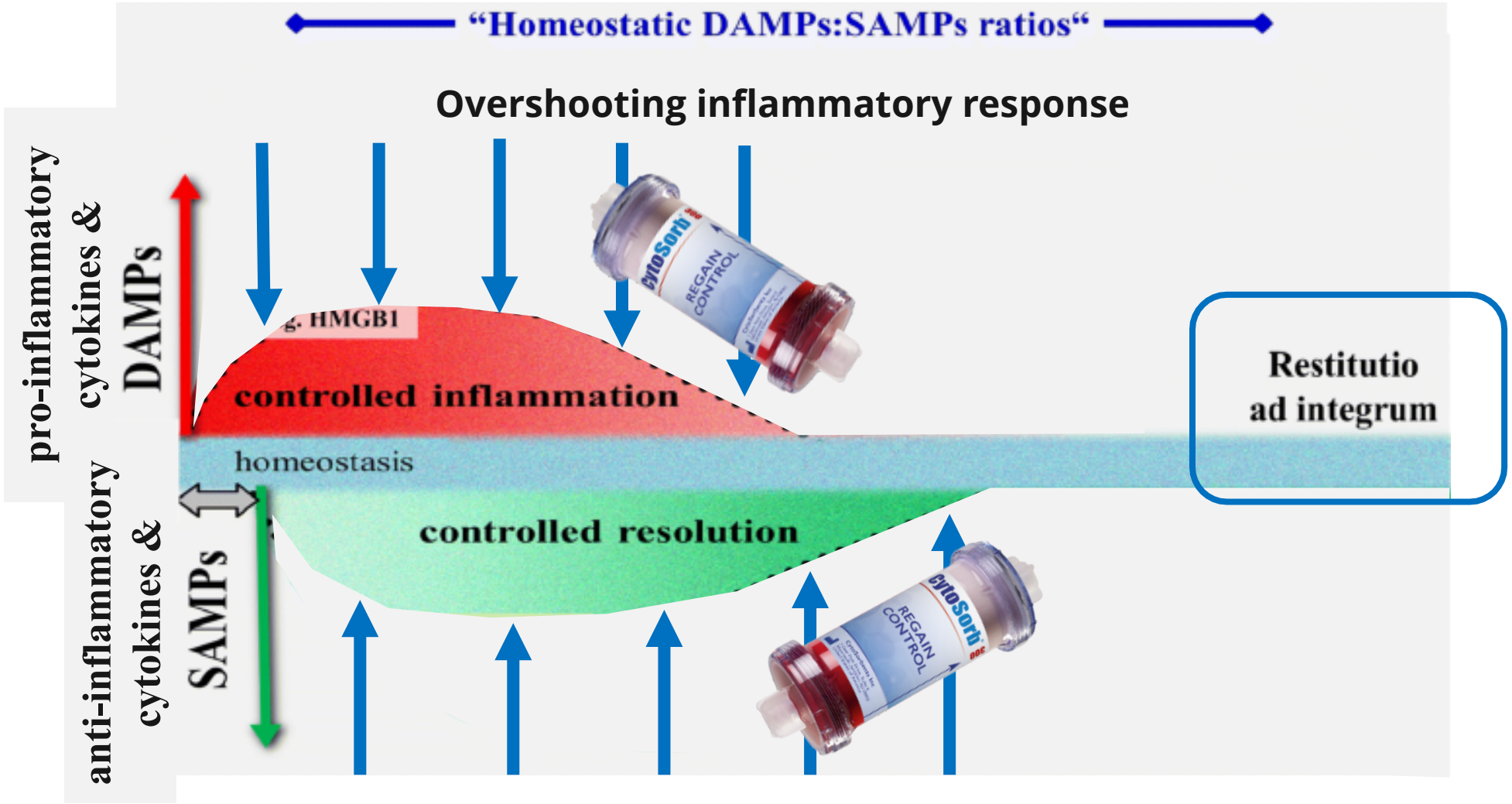
Background

- Sepsis prevalence in cardiac surgery ICU patients is estimated around 2.5%, with an exceptionally high mortality rate, above 65 – 80%[1]
- Up to 50% of patients undergoing cardiac surgery may experience postoperative vasoplegic syndrome (former SIRS)[2]
- SIRS / septic shock in cardiac surgery is associated with high hospital mortality & morbidity
- Pathophysiology: dysregulated release of vasodilatory mediators and cytokines
- Elimination of excessive (toxic!) levels of cytokines with hemoadsorption may improve surgical outcomes by reducing inflammatory response



[1] Ball, L., et al. (2016). "Postoperative complications of patients undergoing cardiac surgery." Curr Opin Crit Care 22(4): 386-392.
[2] Busse, L. W., et al. (2020). "Vasoplegic syndrome following cardiothoracic surgery-review of pathophysiology and update of treatment options." Crit Care 24(1): 36.



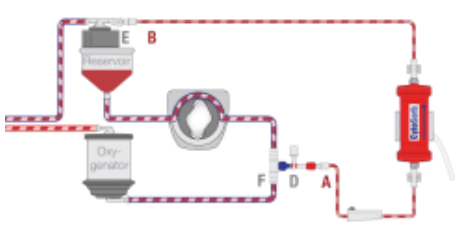
Legend: DAMPs– damage-associated molecular patterns, SAMPs – suppressing/inhibiting DAMPs

Adapted from: *Land, W.G., 2020. Use of DAMPs and SAMPs as Therapeutic Targets or Therapeutics: A Note of Caution. Molecular Diagnosis & Therapy 24, 251–262.. doi:10.1007/s40291-020-00460-z*

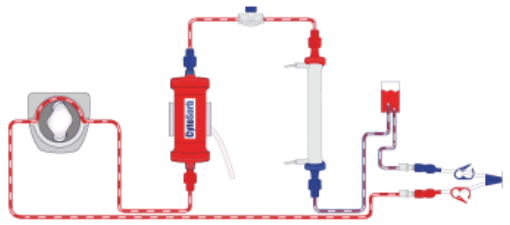
Intra- versus postoperative

Prevention (Therapy)

Therapy



intraoperative

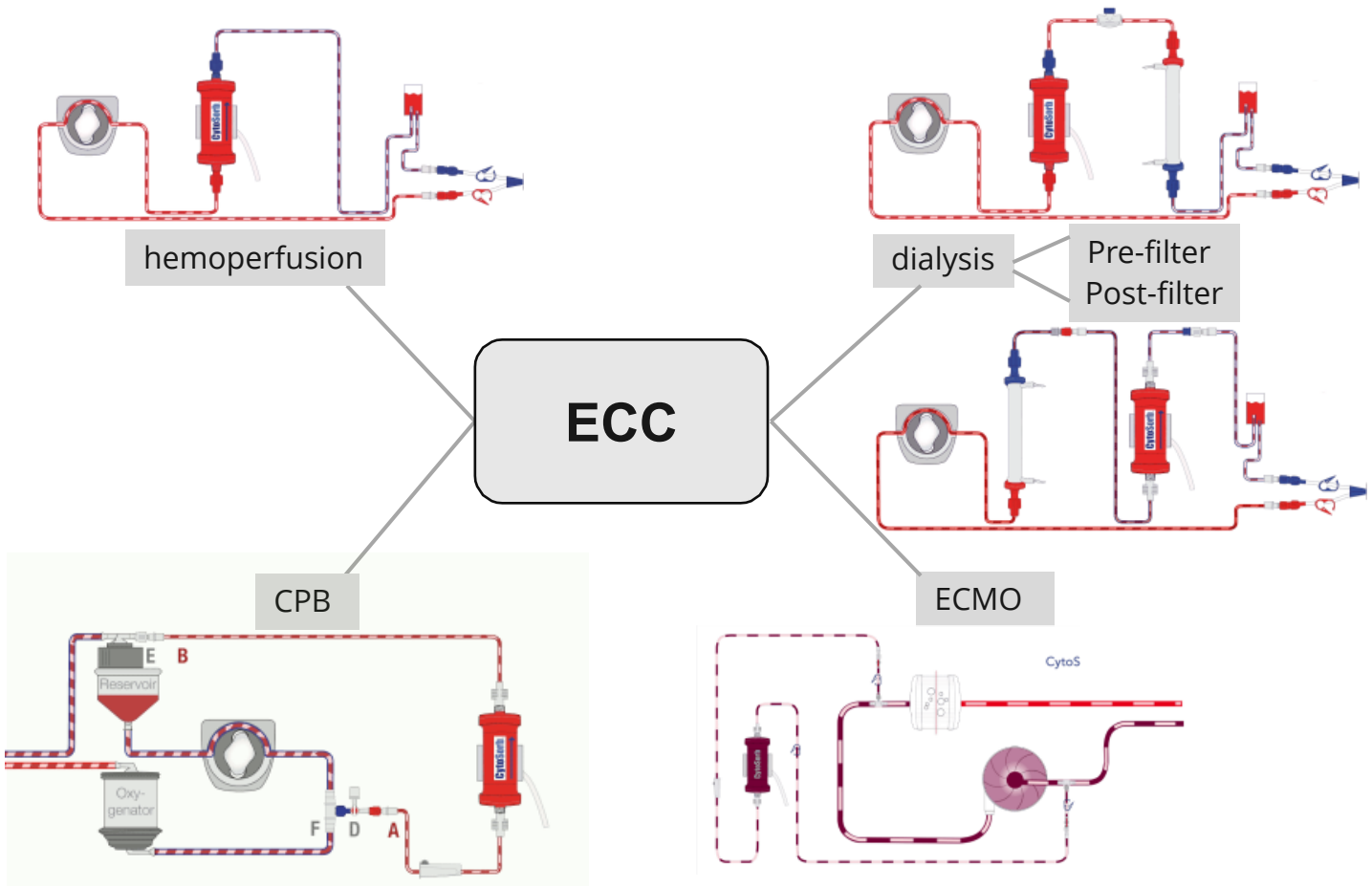


postoperative

If standard therapy based on guidelines fails to give sufficient hemodynamic stabilization within the first 6 to 24 hours, hemoadsorption should be considered as an adjunctive therapy.

SIRS / Sepsis → O_2, volume therapy, cathecholamines,…

Therapy modes



RESEARCH ARTICLE

Extracorporeal cytokine adsorption: Significant reduction of catecholamine requirement in patients with AKI and septic shock after cardiac surgery

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2 Department of Thoracic and Cardiovascular Surgery, West German Heart & Vascular Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany

Artificial Organs

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

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

*Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute; and †Vita-Salute San Raffaele University of Milan, Milan, Italy

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Int J Artif Organs 2016; 39(3): 141-146
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SHORT COMMUNICATION

Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series

Karl Träger[1], Daniel Fritzler[1], Guenther Fischer[1], Janpeter Schröder[1], Christian Skrabal[2], Andreas Liebold[2], Helmut Reinelt[1]

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Short communication

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Karl Träger[1], Christian Skrabal[2], Guenther Fischer[1], Janpeter Schroeder[1], Larissa Marenski[1], Andreas Liebold[2], Helmut Reinelt[1] and Thomas Datzmann[1]

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Artificial Organs

LETTERS TO THE EDITOR

Mechanical circulatory support with Impella 5.0 in septic shock

Zaki Haidari, Arjang Ruhparwar, Alexander Weymann

First published: 14 September 2020 | https://doi.org/10.1111/aor.13793

Open Access Case Report

Urgent Coronary Artery Bypass Grafting Complicated by Systemic Inflammatory Response from Fulminant Herpes Zoster Successfully Managed with Adjunct Extracorporeal Hemoadsorption: A Case Report †

by Zaki Haidari [1], Wilko Weißenberger [1], Bartosz Tyczynski [2], Ender Demircioglu [1], Efthymios Deliargyris [3], Martin Christ [4], Matthias Thielmann [1], Mohamed El Gabry [1], Arjang Ruhparwar [1] and Daniel Wendt [1,*]

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† Presented at the ESC Acute CardioVascular Care 2022, Marseille, France, 18–20 March 2022.

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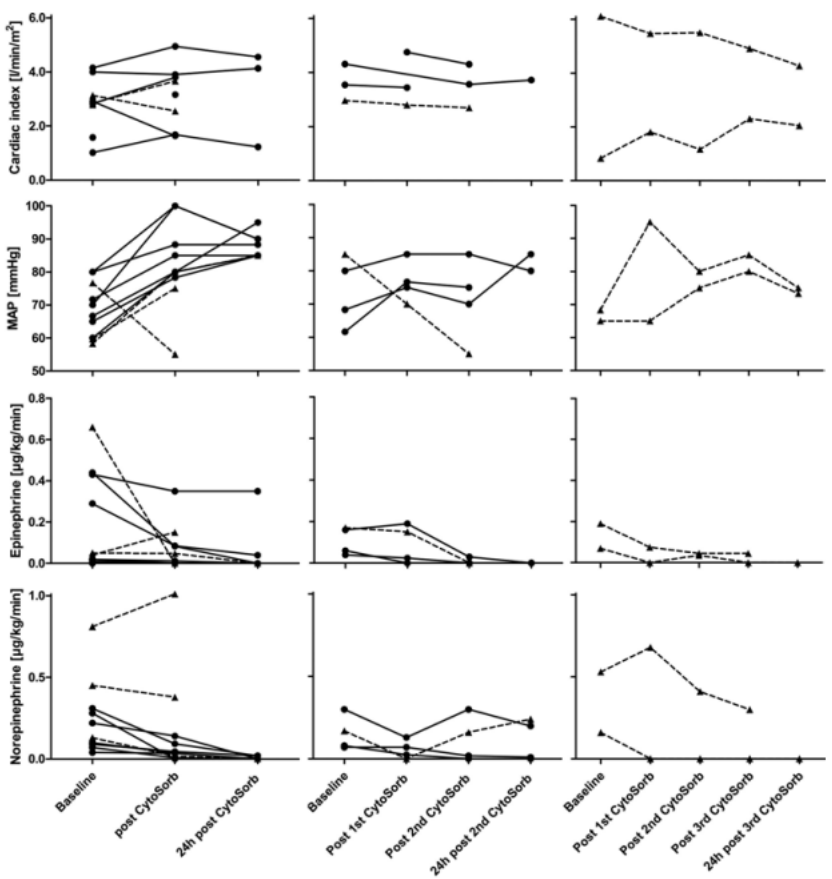
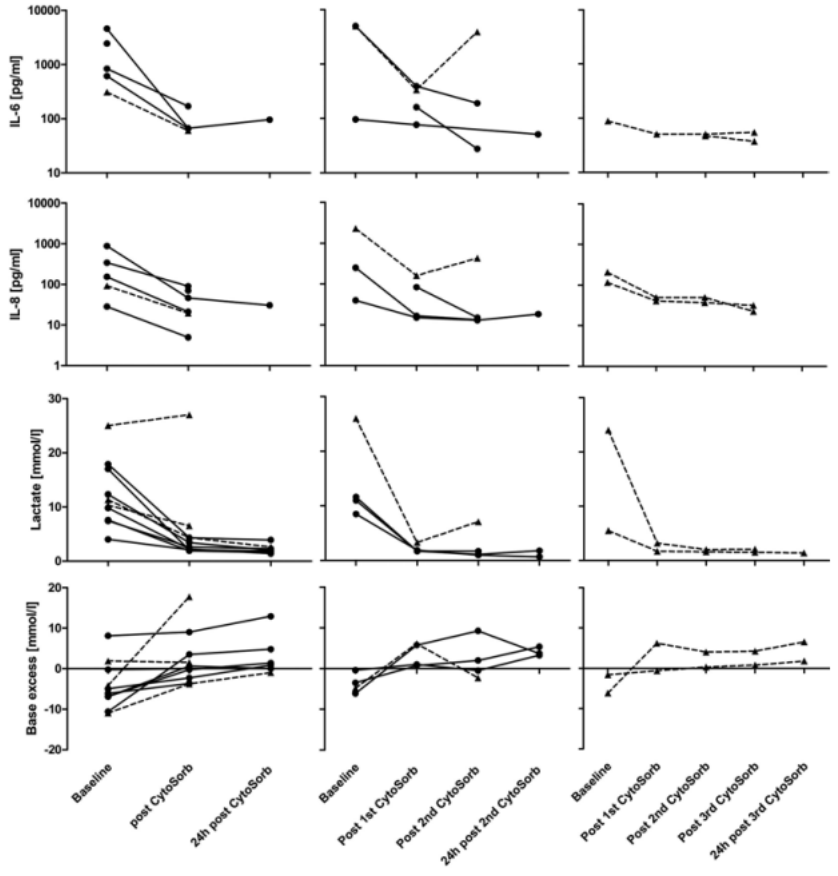
Patient characteristics

Case No	Age (years)	Gender	BMI	CPB time (min)	X clamp time (min)	Type of surgery	Emergency	CytoSorb treatments (*n*)	CytoSorb treatment time (h)	Hydrocortison	APACHE II baseline	Outcome ICU	28 day survival
1	68	M	34.1	107	56	MV replacement	Yes	1	29	Yes	29	Surv	Yes
2	78	M	25.9	120	80	MV repair	No	1	29	Yes	25	Surv	Yes
3	69	M	29.8	235	157	Ascending aorta repair. AV replacement	No	1	32	Yes	18	Surv	Yes
4	63	M	34.4	134	81	AV replacement. CABG	No	1	41	Yes	27	Surv	Yes
5	81	M	28.7	191	139	CABG. MV repair. TV repair. aortic root repair	No	1	33	Yes	24	Surv	Yes
6	75	M	28.7	214	116	Ascending aorta and aortic arch replacement	Yes	1	38	No	47	Died	No
7	75	M	23.9	120	67	MV replacement. TV repair	No	3	38, 25, 25	Yes	32	Died	No
8	62	F	20.2	132	82	MV repair. TV repair	No	2	39, 41	No	24	Surv	Yes
9	73	M	43.2	112	58	Ascending aorta and aortic arch repair	No	2	45, 26	No	34	Died	No
10	53	M	39.6	392	247	Ascending aorta replacement. David surgery	Yes	2	33, 36	No	22	Surv	Yes
11	77	F	27.2	327	178	Redo ascending aorta replacement. AV replacement. CABG	No	3	44, 2, 39	Yes	29	Died	No
12	74	M	37.4	348	168	Ascending aorta replacement. AV replacement. CABG	No	2	29, 24	No	24	Surv	Yes
13	84	M	24.8	230	157	AV and MV replacement. CABG	Yes	1	36	No	36	Died	No
14	55	M	30.8	226	104	Ascending aorta repair	Yes	1	34	No	28	Surv	Yes
15	77	F	19.7	236	125	Ascending aorta and aortic arch repair	No	1	50	Yes	23	Surv	Yes
16	73	F	25	422	112	Aortic root replacement. CABG	Yes	1	5	Yes	36	Died	No

MV = mitral valve; AT = aortic valve; CABG = coronary artery bypass graft; TV = tricuspid valve.

Hemodynamic, inflammatory and metabolic outcome





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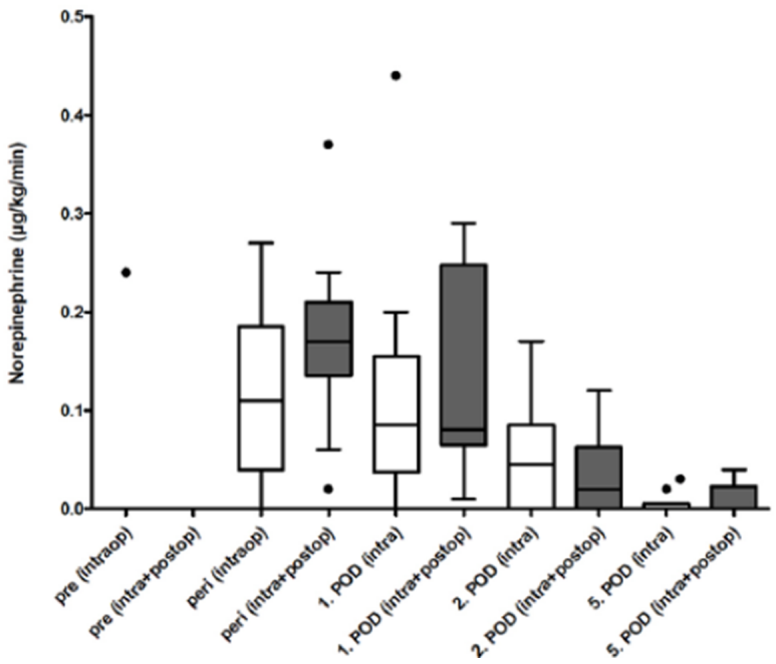
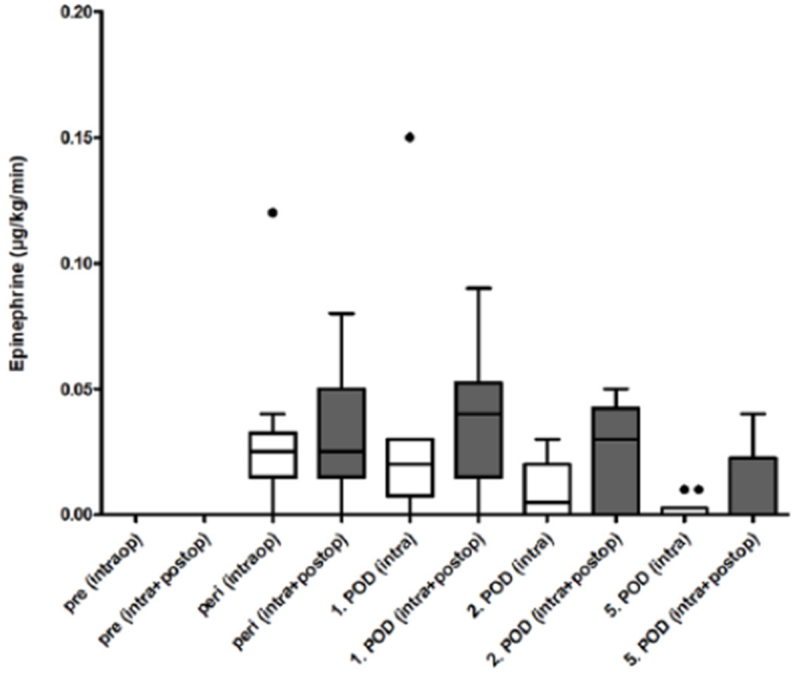
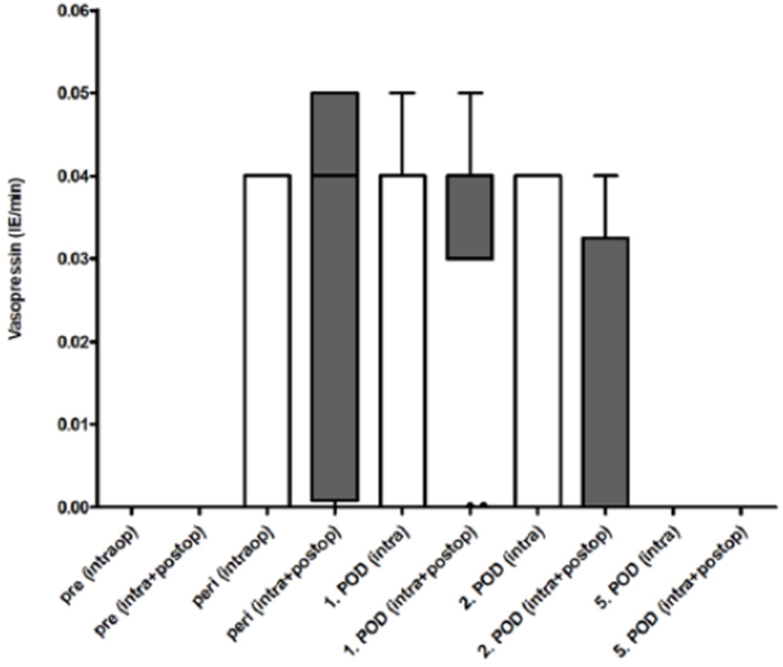
Lars-Uwe Kühne, Robert Binczyk and Friedrich-Christian Rieß

Case No.	Gender (M/F)	Weight (kg)	Age (years)	BMI	Indication and microbiological findings	Emergency procedure (Y/N)	Reoperation (Y/N)	Dialysis dependency pre (Y/N)	EURO score II pre	APACHE II pre	SOFA pre	SOFA (7.POD)	CPB time (min)	Diuresis CPB (mL/kg/min)	CytoSorb treatments (n)	Delay of CVVHD start after admission to ICU (h)	Dialysis days	Ventilator days	Vasopressor days	No. of rethoracotomies	Sternum infection (Y/N)	Stroke (Y/N)	AV block (Y/N)	ICU days	ICU survival (Y/N)	90-day survival (Y/N)
11	M	86	59	24	Aortic valve endocarditis (*E. faecalis*)	Y	Y	N	34.9	25	10	10	250	0.7	1	12	7	7	7	2	N	N	Y	20	Y	Y
12	M	100	72	35	Aortic valve endocarditis (*E. faecalis*)	Y	N	N	24.2	24	10	8	107	0.1	1	1	5	1	5	1	N	N	N	19	Y	Y
13	M	85	57	26	Aortic valve endocarditis (*Proteus mirabilis*)	Y	N	N	24.2	27	14	5	202	1.4	1	6	2	3	6	0	N	N	N	7	Y	Y
14	F	95	82	35	Aortic valve endocarditis (*Streptococcus agalactiae*)	Y	Y	N	55.7	19	11	9	282	0.1	1	2	30	6	15	0	N	N	Y	30	Y	Y
15	M	77	76	25	Aortic and mitral valve endocarditis (*S. aureus*)	N	Y	N	68.7	28	9	14	212	0.2	1	6	7	18	10	1	N	N	N	18	Y	N
16	M	67	75	28	Aortic valve endocarditis (*E. faecalis*)	N	Y	N	63.9	25	10		359	0.7	1	2	3	3	3	1	N	N	N	3	N	N
17	F	62	66	24	Aortic and mitral valve endocarditis (*E. faecalis*)	Y	Y	N	32.7	15	10	14	291	0.5	1	1	20	28	2	0	N	N	N	26	Y	Y
18	M	138	68	45	Mitral valve endocarditis (*Streptococcus dysgalactiae*)	Y	Y	N	42.0	38	12	2	203	0.5	1	2	4	5	4	1	N	N	N	7	Y	Y
19	M	83	72	25	Aortic root abscess (*Staphylococcus epidermidis*)	N	Y	N	18.2	21	14	1	212	0.0	1	3	3	1	2	0	N	N	N	8	Y	Y
20	F	90	76	30	Mitral (bio) valve endocarditis (*S. epidermidis*)	N	Y	N	30.0	14	12	13	338	0.1	1	12	28	1	20	0	N	N	N	30	Y	Y
		85.5	72	27					33.8	24.5	10.5	9	231	0.35	1			04	5.5					18.5		
		62–138	57–82	24–45					18.2–68.7	14–38	9–14	1–14	107–359	0.0–1.4				1–28	2–20					3–30		

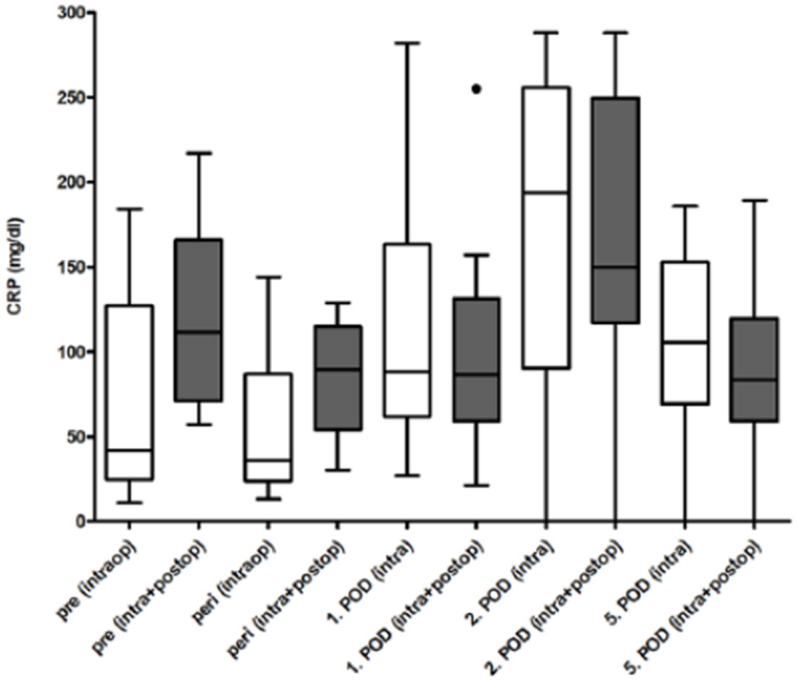
Hemodynamics

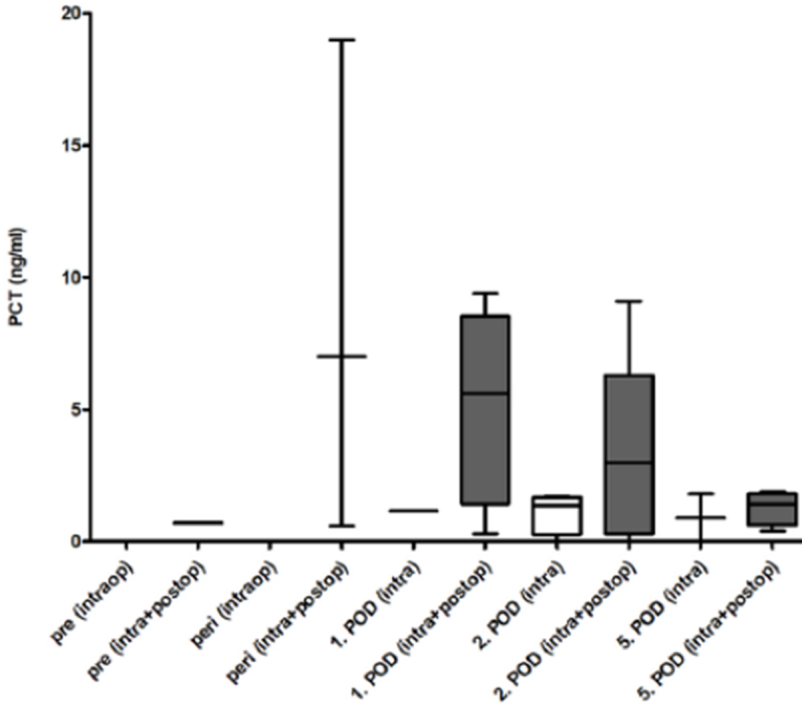


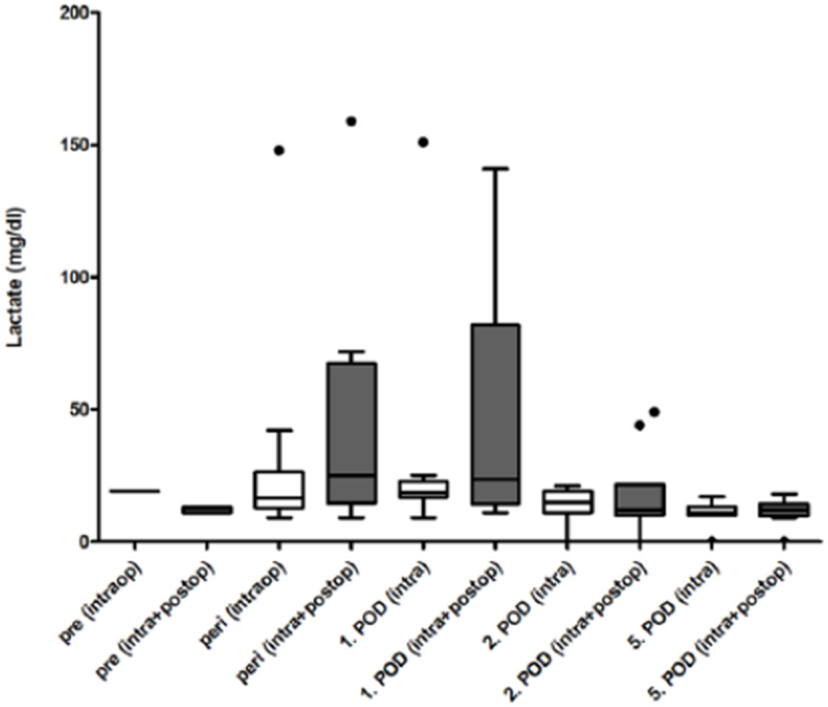




Inflammatory and metabolic outcome







RESEARCH ARTICLE

Extracorporeal cytokine adsorption: Significant reduction of catecholamine requirement in patients with AKI and septic shock after cardiac surgery

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1 Department of Nephrology, University Hospital Essen, University Duisburg-Essen, Essen, Germany,
2 Department of Thoracic and Cardiovascular Surgery, West German Heart & Vascular Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany

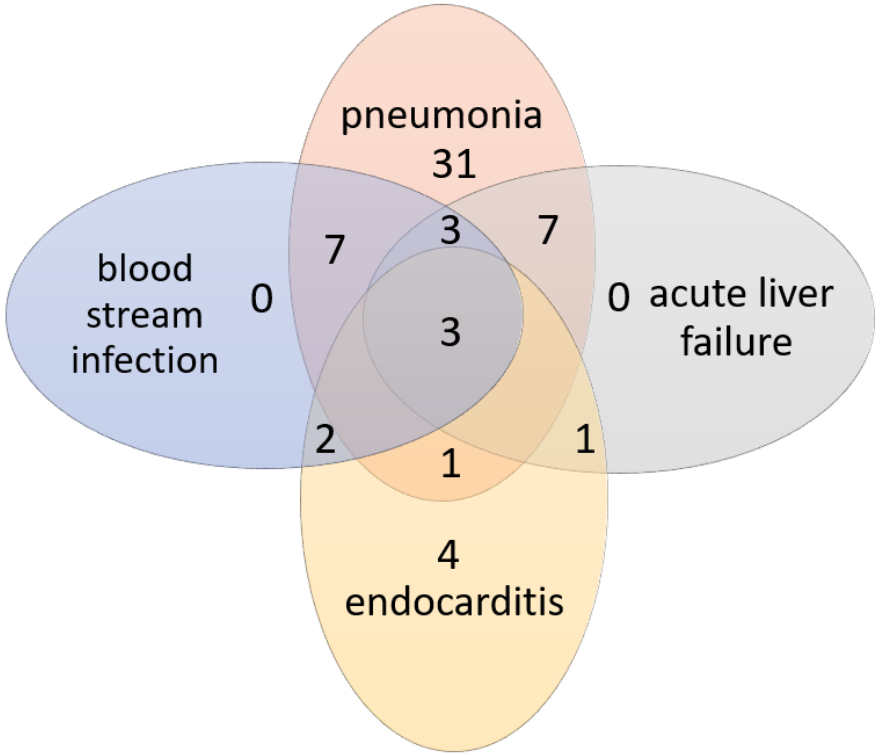
Extracorporeal cytokine adsorption

Methods and patient characteristics

- Retrospective study
- 64 patients with septic shock and AKI after cardiac surgery
  - Pneumonia

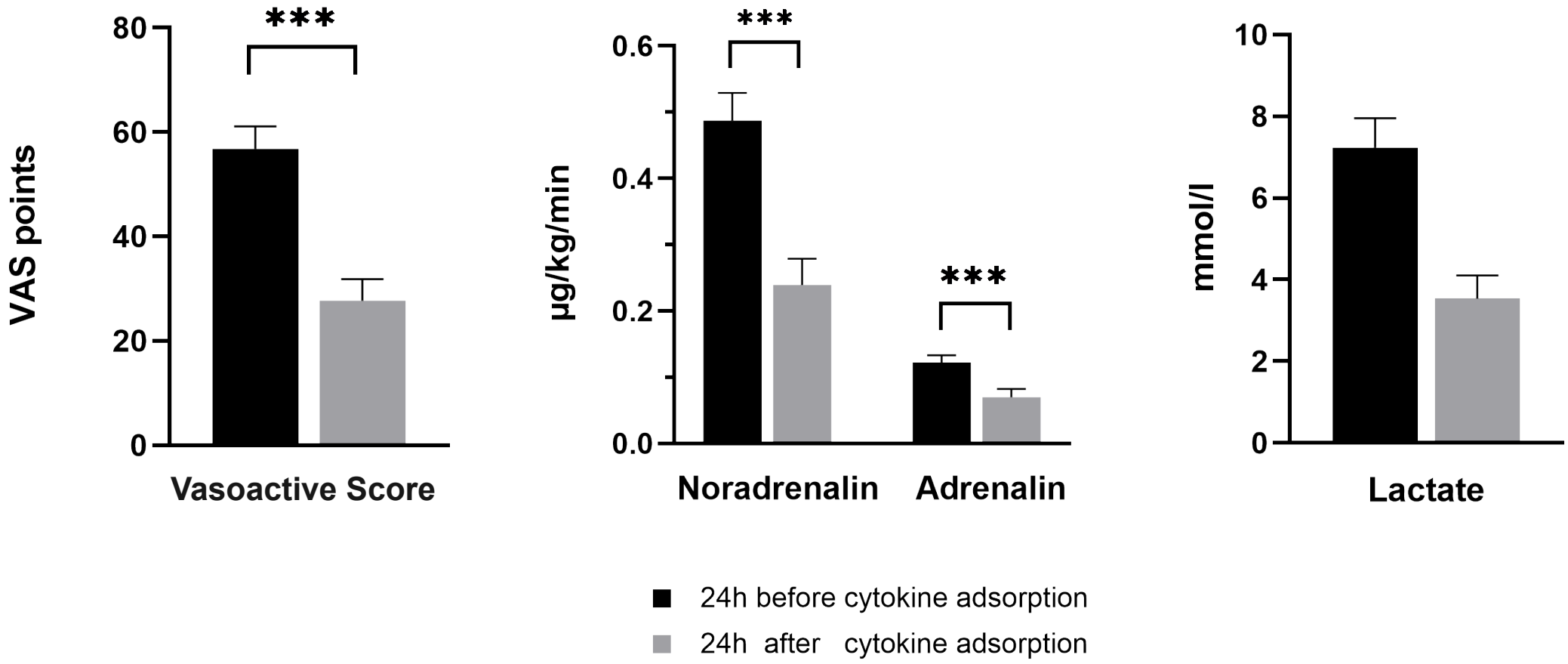
- 58 % Male
- Mean age 67 years (range 46-83 years)

- Cytokine adsorption was applied in addition to continuous renal replacement therapy (CRRT) with citrate anticoagulation in all patients.

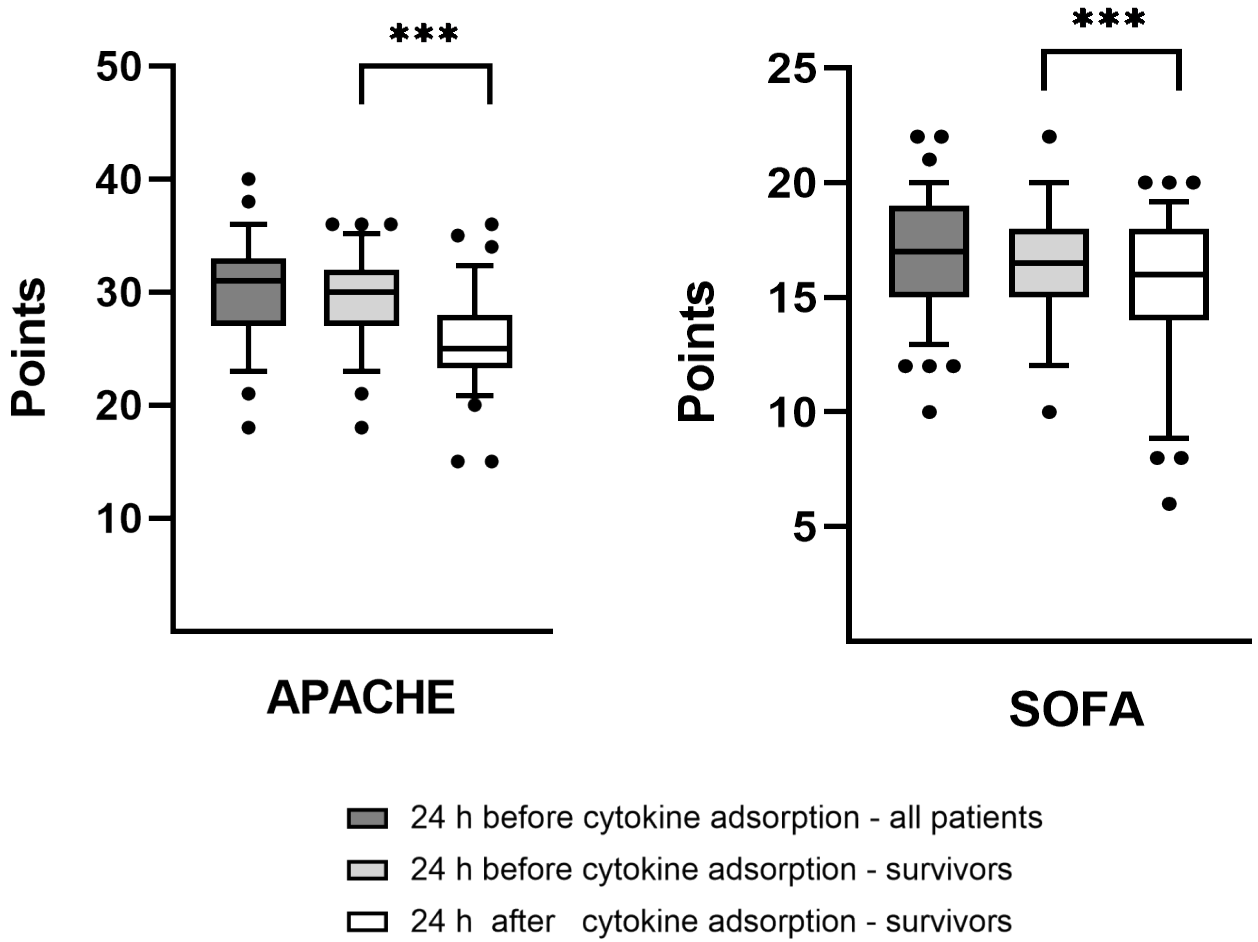


Kristina Boss
Essen, Germany

Hemodynamics



Mortality



- Predicted Mortality:

  SOFA-Score 16,7 Points ≙ 77 %

  APACHE-Score 30,2 Points ≙ 73 %

- **Observed Mortality = 59,2 %**

Highest benefit for high-risk patients!!!

Score	Risk Group	N	rel. VAS Reduction [%]
EuroSCORE II	< 4 %	21	72
	4-9 %	14	68
	≥ 9 %	27	67
APACHE II	18	1	100
	21-24	5	62
	25-29	21	64
	30-34	29	67
	≥ 34	6	73
SOFA	13-14	10	83
	15-16	18	67
	17	13	59
	18-22	21	71

Boss K et al., PLOS One, 2021

Artificial
Organs

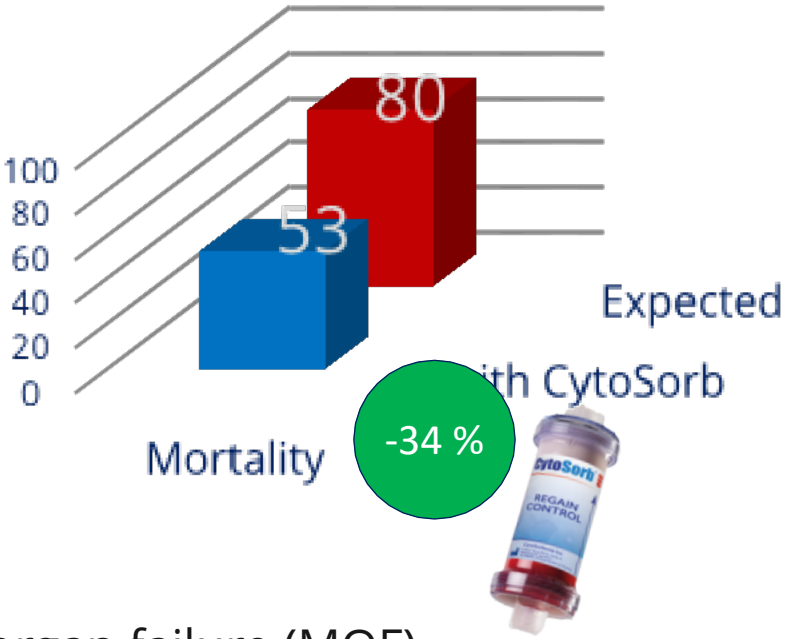
Blood Purification With CytoSorb in Critically Ill Patients: Single-Center Preliminary Experience

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

*Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute; and †Vita-Salute San Raffaele University of Milan, Milan, Italy

TABLE 4. *Laboratory values of 16 patients with total bilirubin ≥10 mg/dL*

Values	Baseline	End of treatment	*P* value
Total bilirubin (mg/dL)	17.1 ± 5	10.8 ± 5.3	0.002
Direct bilirubin (mg/dL)	14.1 ± 4.7	8.9 ± 4.2	0.003
Indirect bilirubin (mg/dL)	3.0 ± 1.8	1.8 ± 1.2	0.04



- 40 patients in cardiac surgery ICU with multiple organ failure (MOF)
- Indications for CytoSorb: hyperbilirubinemia and/or ALF (70%), sepsis or septic shock (20%), SIRS (5%), rhabdomyolysis (5%)
- CytoSorb integration into ECMO (19) or as stand-alone in hemoperfusion mode (21)
- Significant reduction of VIS, as well as bilirubin, lactate, CPK and LDH
- Observed mortality of 53% vs 80% expected (based on SOFA score)

Short communication

IJAO The International Journal of Artificial Organs

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Karl Träger[1], Christian Skrabal[2], Guenther Fischer[1], Janpeter Schroeder[1], Larissa Marenski[1], Andreas Liebold[2], Helmut Reinelt[1] and Thomas Datzmann[1]

- Retrospective case series, 23 pts. on ECLS in combination with CytoSorb
- Heterogeneous patient population with different ECLS indications
- Trigger events: severe hyperinflammatory activation, severe reperfu-sion injury, extended CPB times with post--cardiotomy low cardiac output, and refractory vasoplegic response with rapid progressive organ dysfunction, also severe hemolysis and hyperbilirubinemia

Results:

- Significant reduction of IL-6
- Significant reduction of norepinephrine demand
- Significant reduction of lactate levels

CONCLUSION:

“Due to a modulation of the cytokine response, CytoSorb may offer a potentially promising new treatment option for severe ECLS--related hyperinflamma-tion that presents with hemodynamic instability and requires high doses of vasopressors.”

Artificial Organs

LETTERS TO THE EDITOR

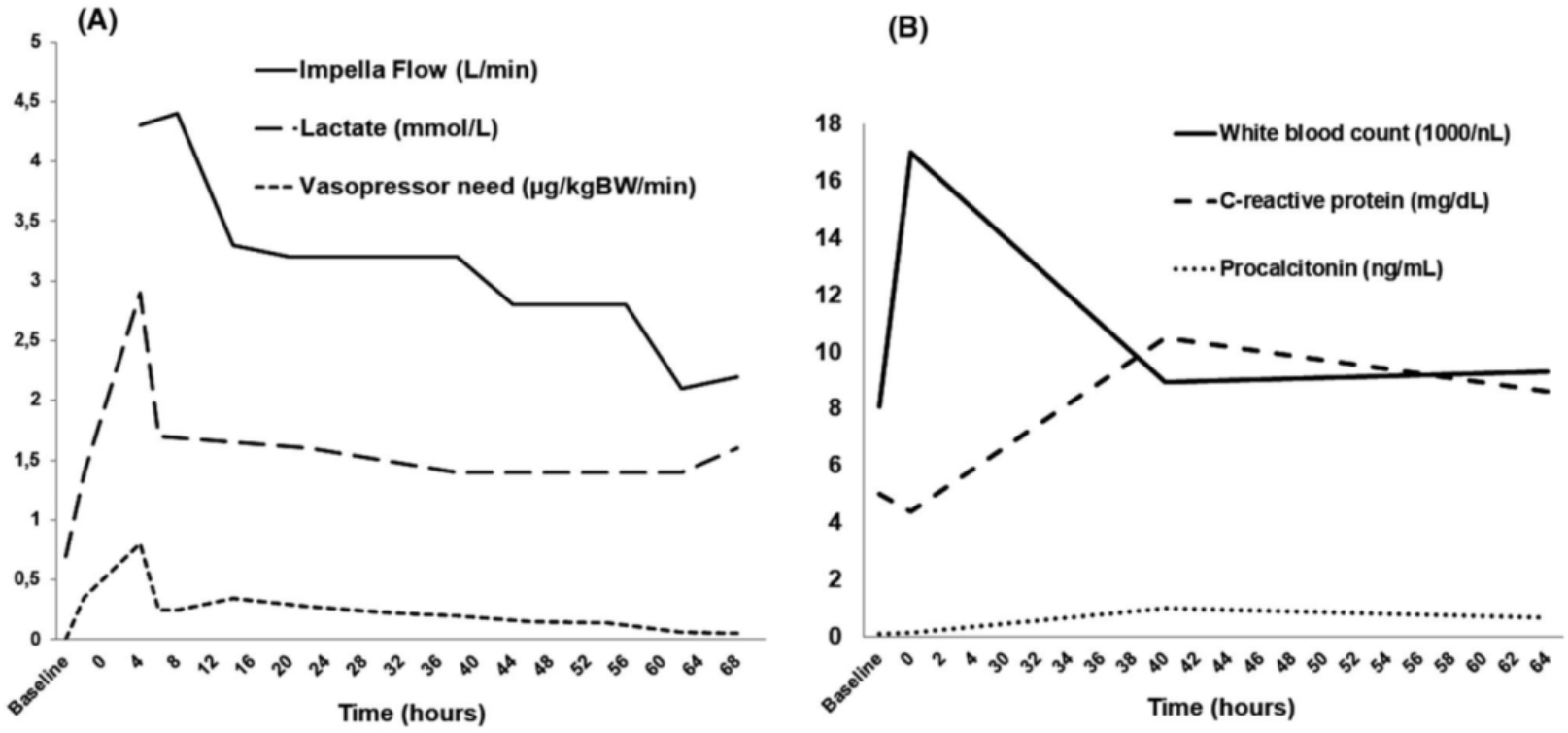
Mechanical circulatory support with Impella 5.0 in septic shock

Zaki Haidari, Arjang Ruhparwar, Alexander Weymann

First published: 14 September 2020 | https://doi.org/10.1111/aor.13793

Case 1

- 71-year-old male
- CHF due to DCM (LVEF: 15%)
  - CRT (11 years ago)
- CDRIE: Staph. lugdunensis
  - Uncontrolled infection
  - Acute renal failure
  - Pulmonary embolisms
  - TLE: unsuccessful (adhesions)
- Surgical lead extraction
  - CPB with hemoadsorption
  - Postoperative: septic shock
    - CRRT including hemoadsorption
    - MCS: Impella 5.0



Open Access Case Report

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[4] Department of Cardiology and Intensive Care Medicine, Knappschaftskrankenhaus Bottrop, 46242 Bottrop, Germany
* Author to whom correspondence should be addressed.
† Presented at the ESC Acute CardioVascular Care 2022, Marseille, France, 18–20 March 2022.

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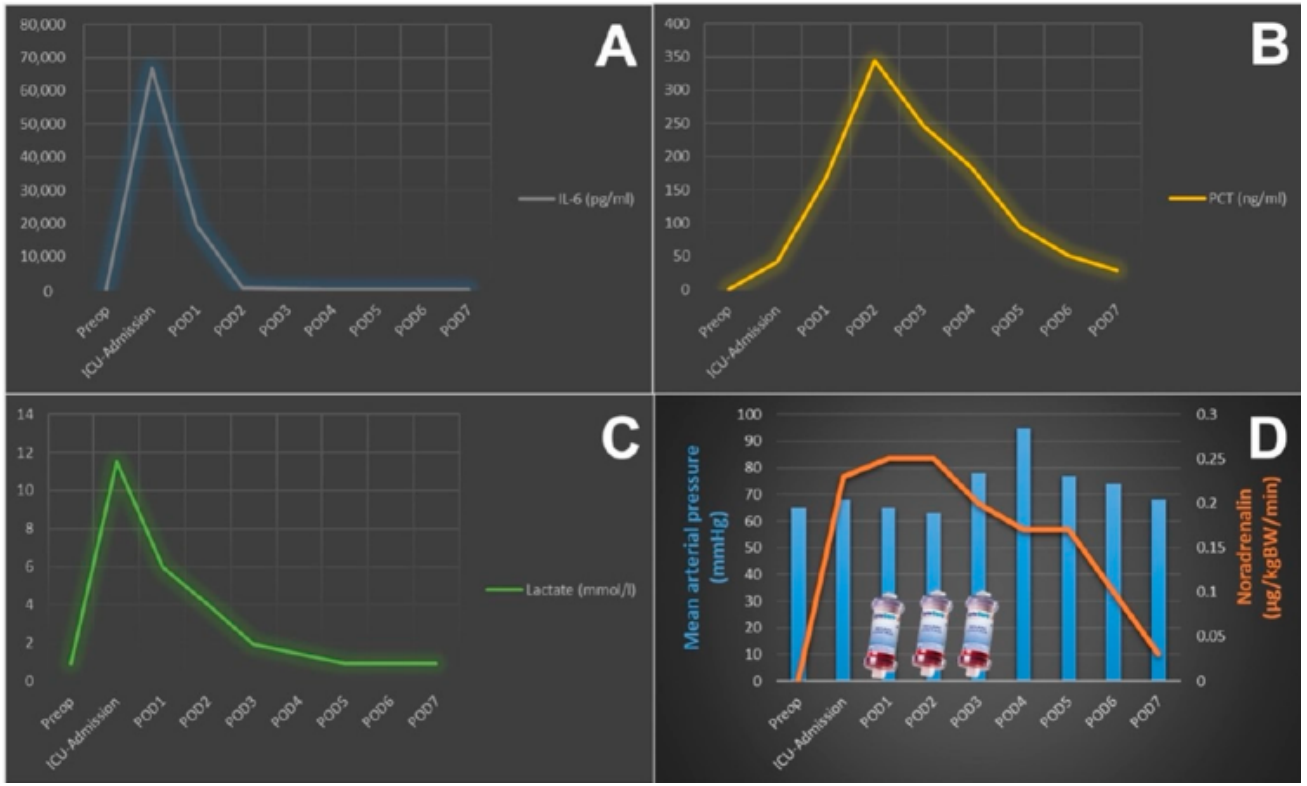
Case 2

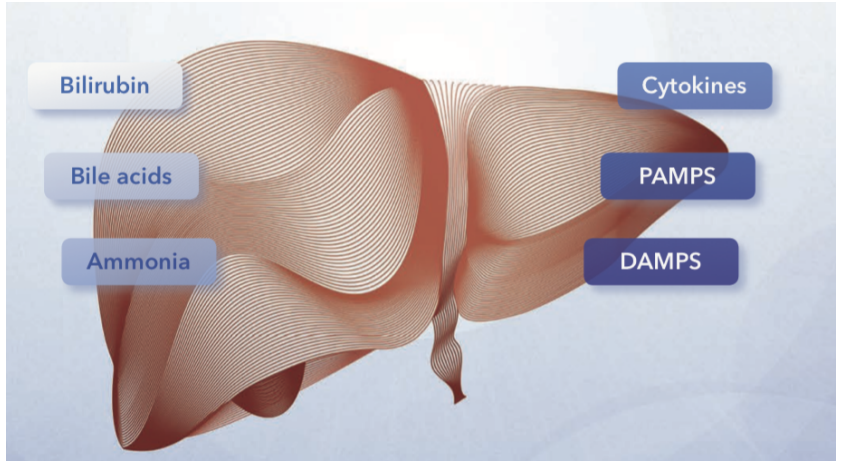
- **56 years, male**
- **Severe COPD and PAD**
- **IAP due 3VD with LM-Stenosis**
  - **Good LV function**
  - **Proximal LSA stenosis: steal syndrome**
- **Herpes zoster**
  - **Aciclovir**
  - **Analgesics and topical therapy**
- **Heparin and Nitro i.v.**
  - **8 days**

CABG

- Anesthesia induction: noradrenalin 0.75 µg/kgBW/min
- Cardiopulmonary bypass: noradrenalin 1.5 µg/kg/BW/min
  - 1000 mg cortisone IV
  - 2mg clemastin IV
  - Volume therapy: fluid balance +8.5 L
  - Additional dose of 500 mg aciclovir
  - 8 units of RBC
  - 4 units of platelets
  - 5000 IE of prothrombin complex concentrate
  - 16g of fibrinogen
- Hemoadsorption: intra- and postoperative (CRRT)
- ECMO
  - Veno-arterial till POD 2
  - Veno-venous till POD 15
- Clinical Follow-up at 6 months: asymptomatic and active

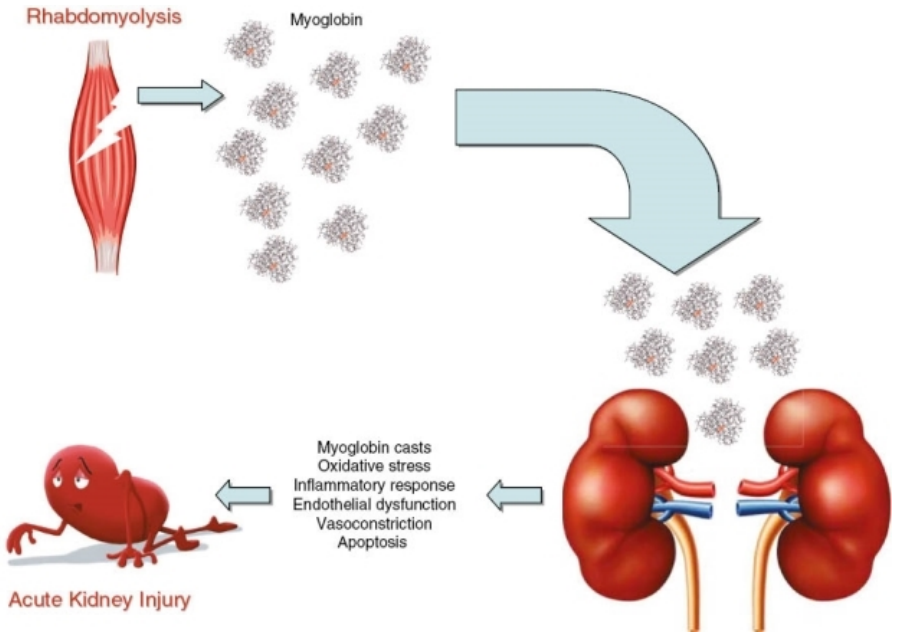


What about other complications?



- The incidence of liver failure postcardiac surgery is 4%, but as many as 10% of patients who received cardiopulmonary bypass (CPB) experience some level of hepatic injury.[1]

- Rhabdomyolysis is not a frequent postcardiac surgery complication, but more than 40% of patients with rhabdomyolysis develop AKI.[2]



Adapted from:
Lippi et al. Serum myoglobin immunoassays: obsolete or still clinically useful?" Clinical Chemistry and Laboratory Medicine (CCLM), vol. 54, no. 10, 2016, pp. 1541-1543.

[1] *Chacon et Schulte, Liver Dysfunction in Cardiac Surgery – What Causes It and Is There Anything We Can Do? Jour Cardiovasc Anesth*
[2] *Omar et al., Rhabdomyolysis following Cardiac Surgery: A Prospective, Descriptive, Single-Center Study. Biomed Res Int. 2016*

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Successful elimination of bilirubin in critically ill patients with acute liver dysfunction using a cytokine adsorber and albumin dialysis: a pilot study

Christina Scharf[1]✉, Uwe Liebchen[1], Michael Paal[2], Andrea Becker-Pennrich[1], Michael Irlbeck[1], Michael Zoller[1] & Ines Schroeder[1]

- Retrospective case series, 39 pts with acute liver dysfunction (ALD) and corresponding high levels of bilirubin (>10 mg/dl)
- CytoSorb integrated into high flux dialysis (№ 33) vs. Advanced organ support system ADVOS (№ 6)
- Significant and comparable decrease in bilirubin in critically ill patients by both CytoSorb and ADVOS

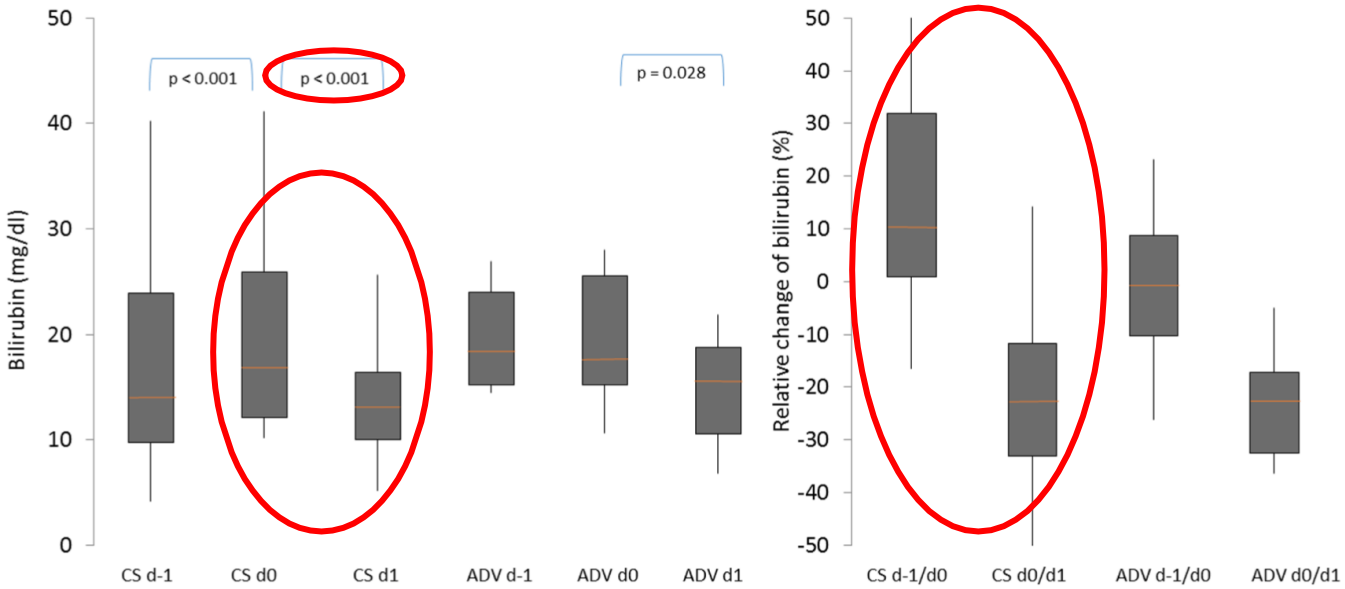


Figure 2. Development and relative reduction in bilirubin levels in patients with CytoSorb and ADVOS therapy. d–1: day before treatment, d0: shortly before treatment, d1: directly after treatment, CS: CytoSorb, ADV: advanced organ support; orange line represents the median, grey boxes the interquartile range and the whiskers are limited to 1.5 times the interquartile range.

"An advantage of CS is its easy integration into high-flux dialysis, which allows its use at smaller hospitals."

Scharf *et al. Crit Care* (2021) 25:41
https://doi.org/10.1186/s13054-021-03468-x

Critical Care

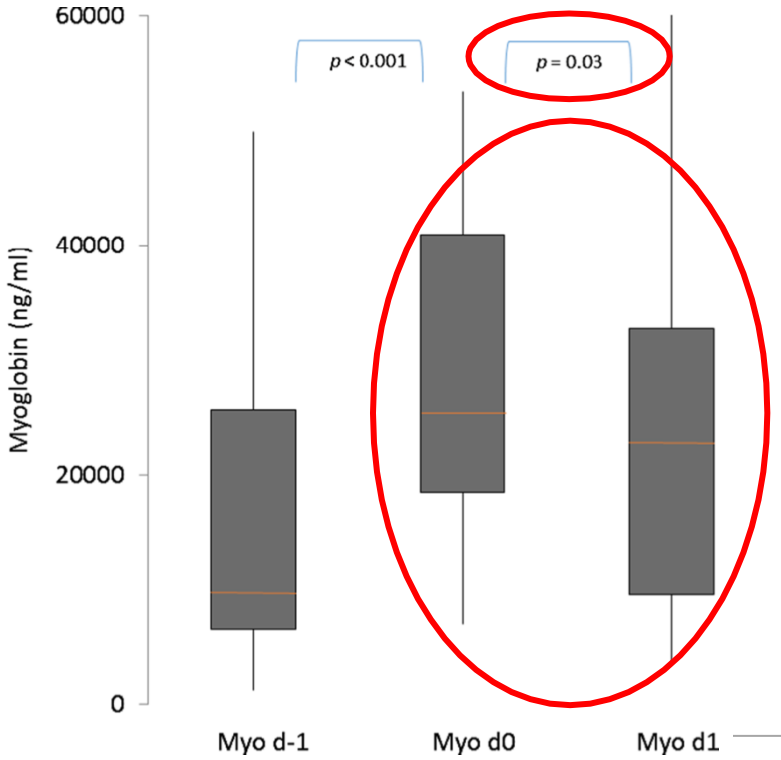
RESEARCH

Open Access

Blood purification with a cytokine adsorber for the elimination of myoglobin in critically ill patients with severe rhabdomyolysis

Christina Scharf[1*], Uwe Liebchen[1], Michael Paal[2], Michael Irlbeck[1], Michael Zoller[1] and Ines Schroeder[1]

- Retrospective case series, 43 pts with anuric renal failure
- Massive rhabdomyolysis (med. myoglobin level > 25,000 ng/ml)
- 22 pts (51%) with ongoing rhabdomyolysis
- 1/3 of pts on ECMO
- SOFA score was 19 (expected mortality > 90%)



Results:

- Significant reduction of myoglobin (a median relative reduction rate of 29%)
- Observed in-hospital mortality vs. SAPS II score-predicted was 67.4% and 92.5%, respectively)

"In summary, myoglobin removal with the cytokine adsorber CS integrated into a high-flux dialyzer can be recommended for clinical routine due to its existing CE mark, ease of use and absence of side effects."

Summary

CytoSorb therapy post cardiac surgery - in whom?

Patients not responding to standard therapy for:

- Severe systemic hyperinflammation (SIRS) complicated with vasoplegia
- Septic shock
- Endocarditis with high-grade intraoperative findings, development of AKI, and increasing vasopressor demand
- Severe hyperbilirubinemia
- Severe myoglobinemia

CytoSorb therapy post cardiac surgery - in whom, when?

- 6 – 24 hrs. after the diagnosis (of refractory shock or non-response to standard of care)
- Norepinephrine requirement > 0.3 µg/kg/min (or use of 2 or more vasopressors)
- IL-6 > 300 – 500 pg/mL*
- Poor lactate clearance
- In liver dysfunction, bilirubin ≥ 10 mg/dL (> 170 µmol/L)
- In rhabdomyolysis, myoglobin ≥ 10,000 ng/mL

** Depending on the clinical picture and disease progression*

CytoSorb therapy post cardiac surgery - in whom, when and how?

- Anticoagulation as usual
- Stand-alone configuration / hemoperfusion mode
- (C)RRT
- ECMO / ECLS
- Max 24 hrs. per adsorber
- Blood flow through CytoSorb: 100 – 700 ml/min

Conclusions

- Hemoadsorption as an adjunct therapy in the postoperative course of high-risk cardiac surgery patients seems to provide:
  - hemodynamic stabilization in sepsis/SIRS (reduced VIS and/or vasopressor demand)
  - improved tissue perfusion (reduced lactate levels)
  - support liver and kidney function (reduced bilirubin and myoglobin levels)

- Limitations:
  - data based on retrospective small studies

Prospective studies with well-defined patient selection criteria and therapy timing and duration are needed to evaluate the role of hemoadsorption with CytoSorb in high-risk cardiac surgical patients.