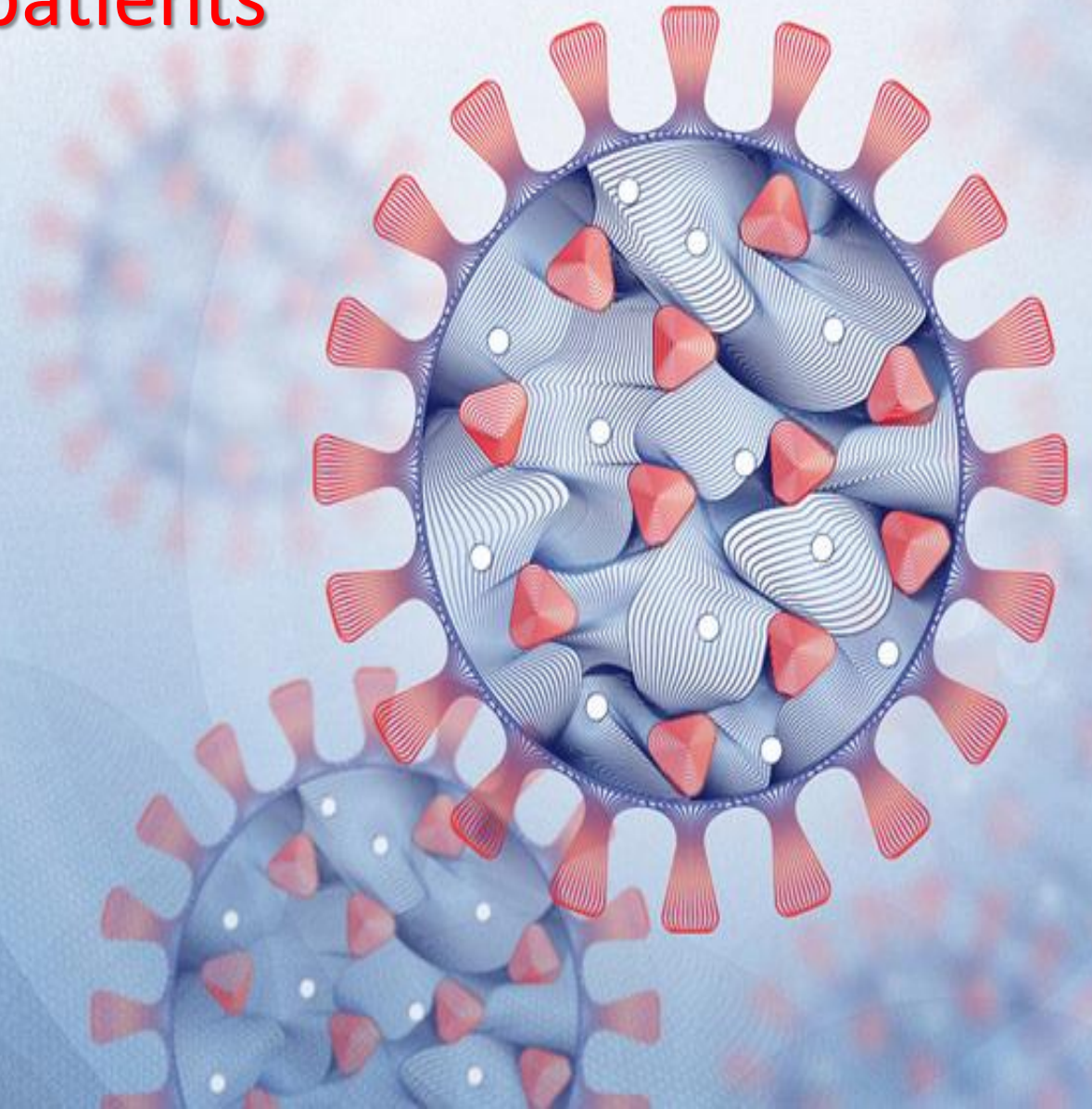


# Hemoperfusion in critically ill patients with COVID-19

Ata Mahmoodpoor.MD.FCCM  
Professor of Anesthesiology  
TBZMed, 2021



# Crises in Intensive Care Medicine!

## Reliance for evidence on RCT

- Mortality as primarily clinical end point?
- Propensity weighted trials

# Sepsis biomarkers: a review

Charalampos Pierrakos, Jean-Louis Vincent\*

Critical Care 2010, 14:R15

**Table 1 Cytokine/chemokines**  
Sepsis marker

IL-1
IL-2
IL-6
IL-8
IL-10
IL-12
IL-15
IL-17
IL-18
IL-20
IL-21
IL-22
IL-23
IL-24
IL-25
IL-26
IL-27
IL-28
IL-29
IL-30
IL-31
IL-32
IL-33
IL-34
IL-35
IL-36
IL-37
IL-38
IL-39
IL-40
IL-41
IL-42
IL-43
IL-44
IL-45
IL-46
IL-47
IL-48
IL-49
IL-50
IL-51
IL-52
IL-53
IL-54
IL-55
IL-56
IL-57
IL-58
IL-59
IL-60
IL-61
IL-62
IL-63
IL-64
IL-65
IL-66
IL-67
IL-68
IL-69
IL-70
IL-71
IL-72
IL-73
IL-74
IL-75
IL-76
IL-77
IL-78
IL-79
IL-80
IL-81
IL-82
IL-83
IL-84
IL-85
IL-86
IL-87
IL-88
IL-89
IL-90
IL-91
IL-92
IL-93
IL-94
IL-95
IL-96
IL-97
IL-98
IL-99
IL-100
IL-101
IL-102
IL-103
IL-104
IL-105
IL-106
IL-107
IL-108
IL-109
IL-110
IL-111
IL-112
IL-113
IL-114
IL-115
IL-116
IL-117
IL-118
IL-119
IL-120
IL-121
IL-122
IL-123
IL-124
IL-125
IL-126
IL-127
IL-128
IL-129
IL-130
IL-131
IL-132
IL-133
IL-134
IL-135
IL-136
IL-137
IL-138
IL-139
IL-140
IL-141
IL-142
IL-143
IL-144
IL-145
IL-146
IL-147
IL-148
IL-149
IL-150
IL-151
IL-152
IL-153
IL-154
IL-155
IL-156
IL-157
IL-158
IL-159
IL-160
IL-161
IL-162
IL-163
IL-164
IL-165
IL-166
IL-167
IL-168
IL-169
IL-170
IL-171
IL-172
IL-173
IL-174
IL-175
IL-176
IL-177
IL-178
IL-179
IL-180
IL-181
IL-182
IL-183
IL-184
IL-185
IL-186
IL-187
IL-188
IL-189
IL-190
IL-191
IL-192
IL-193
IL-194
IL-195
IL-196
IL-197
IL-198
IL-199
IL-200
IL-201
IL-202
IL-203
IL-204
IL-205
IL-206
IL-207
IL-208
IL-209
IL-210
IL-211
IL-212
IL-213
IL-214
IL-215
IL-216
IL-217
IL-218
IL-219
IL-220
IL-221
IL-222
IL-223
IL-224
IL-225
IL-226
IL-227
IL-228
IL-229
IL-230
IL-231
IL-232
IL-233
IL-234
IL-235
IL-236
IL-237
IL-238
IL-239
IL-240
IL-241
IL-242
IL-243
IL-244
IL-245
IL-246
IL-247
IL-248
IL-249
IL-250
IL-251
IL-252
IL-253
IL-254
IL-255
IL-256
IL-257
IL-258
IL-259
IL-260
IL-261
IL-262
IL-263
IL-264
IL-265
IL-266
IL-267
IL-268
IL-269
IL-270
IL-271
IL-272
IL-273
IL-274
IL-275
IL-276
IL-277
IL-278
IL-279
IL-280
IL-281
IL-282
IL-283
IL-284
IL-285
IL-286
IL-287
IL-288
IL-289
IL-290
IL-291
IL-292
IL-293
IL-294
IL-295
IL-296
IL-297
IL-298
IL-299
IL-300
IL-301
IL-302
IL-303
IL-304
IL-305
IL-306
IL-307
IL-308
IL-309
IL-310
IL-311
IL-312
IL-313
IL-314
IL-315
IL-316
IL-317
IL-318
IL-319
IL-320
IL-321
IL-322
IL-323
IL-324
IL-325
IL-326
IL-327
IL-328
IL-329
IL-330
IL-331
IL-332
IL-333
IL-334
IL-335
IL-336
IL-337
IL-338
IL-339
IL-340
IL-341
IL-342
IL-343
IL-344
IL-345
IL-346
IL-347
IL-348
IL-349
IL-350
IL-351
IL-352
IL-353
IL-354
IL-355
IL-356
IL-357
IL-358
IL-359
IL-360
IL-361
IL-362
IL-363
IL-364
IL-365
IL-366
IL-367
IL-368
IL-369
IL-370
IL-371
IL-372
IL-373
IL-374
IL-375
IL-376
IL-377
IL-378
IL-379
IL-380
IL-381
IL-382
IL-383
IL-384
IL-385
IL-386
IL-387
IL-388
IL-389
IL-390
IL-391
IL-392
IL-393
IL-394
IL-395
IL-396
IL-397
IL-398
IL-399
IL-400
IL-401
IL-402
IL-403
IL-404
IL-405
IL-406
IL-407
IL-408
IL-409
IL-410
IL-411
IL-412
IL-413
IL-414
IL-415
IL-416
IL-417
IL-418
IL-419
IL-420
IL-421
IL-422
IL-423
IL-424
IL-425
IL-426
IL-427
IL-428
IL-429
IL-430
IL-431
IL-432
IL-433
IL-434
IL-435
IL-436
IL-437
IL-438
IL-439
IL-440
IL-441
IL-442
IL-443
IL-444
IL-445
IL-446
IL-447
IL-448
IL-449
IL-450
IL-451
IL-452
IL-453
IL-454
IL-455
IL-456
IL-457
IL-458
IL-459
IL-460
IL-461
IL-462
IL-463
IL-464
IL-465
IL-466
IL-467
IL-468
IL-469
IL-470
IL-471
IL-472
IL-473
IL-474
IL-475
IL-476
IL-477
IL-478
IL-479
IL-480
IL-481
IL-482
IL-483
IL-484
IL-485
IL-486
IL-487
IL-488
IL-489
IL-490
IL-491
IL-492
IL-493
IL-494
IL-495
IL-496
IL-497
IL-498
IL-499
IL-500
IL-501
IL-502
IL-503
IL-504
IL-505
IL-506
IL-507
IL-508
IL-509
IL-510
IL-511
IL-512
IL-513
IL-514
IL-515
IL-516
IL-517
IL-518
IL-519
IL-520
IL-521
IL-522
IL-523
IL-524
IL-525
IL-526
IL-527
IL-528
IL-529
IL-530
IL-531
IL-532
IL-533
IL-534
IL-535
IL-536
IL-537
IL-538
IL-539
IL-540
IL-541
IL-542
IL-543
IL-544
IL-545
IL-546
IL-547
IL-548
IL-549
IL-550
IL-551
IL-552
IL-553
IL-554
IL-555
IL-556
IL-557
IL-558
IL-559
IL-560
IL-561
IL-562
IL-563
IL-564
IL-565
IL-566
IL-567
IL-568
IL-569
IL-570
IL-571
IL-572
IL-573
IL-574
IL-575
IL-576
IL-577
IL-578
IL-579
IL-580
IL-581
IL-582
IL-583
IL-584
IL-585
IL-586
IL-587
IL-588
IL-589
IL-590
IL-591
IL-592
IL-593
IL-594
IL-595
IL-596
IL-597
IL-598
IL-599
IL-600
IL-601
IL-602
IL-603
IL-604
IL-605
IL-606
IL-607
IL-608
IL-609
IL-610
IL-611
IL-612
IL-613
IL-614
IL-615
IL-616
IL-617
IL-618
IL-619
IL-620
IL-621
IL-622
IL-623
IL-624
IL-625
IL-626
IL-627
IL-628
IL-629
IL-630
IL-631
IL-632
IL-633
IL-634
IL-635
IL-636
IL-637
IL-638
IL-639
IL-640
IL-641
IL-642
IL-643
IL-644
IL-645
IL-646
IL-647
IL-648
IL-649
IL-650
IL-651
IL-652
IL-653
IL-654
IL-655
IL-656
IL-657
IL-658
IL-659
IL-660
IL-661
IL-662
IL-663
IL-664
IL-665
IL-666
IL-667
IL-668
IL-669
IL-670
IL-671
IL-672
IL-673
IL-674
IL-675
IL-676
IL-677
IL-678
IL-679
IL-680
IL-681
IL-682
IL-683
IL-684
IL-685
IL-686
IL-687
IL-688
IL-689
IL-690
IL-691
IL-692
IL-693
IL-694
IL-695
IL-696
IL-697
IL-698
IL-699
IL-700
IL-701
IL-702
IL-703
IL-704
IL-705
IL-706
IL-707
IL-708
IL-709
IL-710
IL-711
IL-712
IL-713
IL-714
IL-715
IL-716
IL-717
IL-718
IL-719
IL-720
IL-721
IL-722
IL-723
IL-724
IL-725
IL-726
IL-727
IL-728
IL-729
IL-730
IL-731
IL-732
IL-733
IL-734
IL-735
IL-736
IL-737
IL-738
IL-739
IL-740
IL-741
IL-742
IL-743
IL-744
IL-745
IL-746
IL-747
IL-748
IL-749
IL-750
IL-751
IL-752
IL-753
IL-754
IL-755
IL-756
IL-757
IL-758
IL-759
IL-760
IL-761
IL-762
IL-763
IL-764
IL-765
IL-766
IL-767
IL-768
IL-769
IL-770
IL-771
IL-772
IL-773
IL-774
IL-775
IL-776
IL-777
IL-778
IL-779
IL-780
IL-781
IL-782
IL-783
IL-784
IL-785
IL-786
IL-787
IL-788
IL-789
IL-790
IL-791
IL-792
IL-793
IL-794
IL-795
IL-796
IL-797
IL-798
IL-799
IL-800
IL-801
IL-802
IL-803
IL-804
IL-805
IL-806
IL-807
IL-808
IL-809
IL-810
IL-811
IL-812
IL-813
IL-814
IL-815
IL-816
IL-817
IL-818
IL-819
IL-820
IL-821
IL-822
IL-823
IL-824
IL-825
IL-826
IL-827
IL-82



Innovative therapy needs innovation  
based on pathophysiology and the reality of  
ICU to demonstrate efficacy.

Conventional therapies: drugs, magic bullets (e.g. APC)  
Conventional measurements: hemodynamics, biomarkers  
Conventional study design: Randomized Controlled Trials (RCT)

***nothing works!!***

Innovative therapy: Cytosorbents  
Innovative measurements: Microcirculatory imaging  
Innovative study design: sIPTW propensity scoring

stabilized Inverse Probability of Treatment Weights

- Cytokine leads to organ failure
- Blockade of 1 cytokine vs cytokines
- Controlling the inflammatory response may be as important as targeting the virus.

# Attenuation of cytokine storm

- Disease complication
- Multi organ failure
- Duration of symptoms
  
- But what is the best tool and do we use it?
- Traditional therapies
- Like bringing knife to a gun fight
- Some times we need better, stronger and smarter therapies

# Evolution of CRRT Technology



1980

CAVA-CAVHD      CVVA-CVVHD

Focus on Rheology, Membrane and Filter Technology

Focus on Mechanical Circulation and Adoptive Technology

1990

First generation CRRT machines  
CVVH  
CVVHD  
CVVHDF



1995

Second generation CRRT machines  
CVVH  
CVVHD  
CVVHDF and studies on Dose and Adequacy 35 mL/Kg/h

2000

Third generation CRRT machines  
HVHF and HCO Membr.



2005

Liver support  
MOST, CPFA

2010

Lung support  
ECCO2R  
Cutrate  
Endotoxin and Cytokine Removal.  
Sorbent Hemoperfusion



2020

ECOS



# Blood purification techniques

## Proof of concept

Removal of harmful substances  
WBC reprogramming

## Clinical benefit

Decreased need for vasopressors  
Less organ dysfunction  
(Survival ?)

## Potential complications

Removal of other substances  
(nutrient, vitamins, trace elements, antibiotics...)  
Invasiveness  
Bleeding




- **Hemoperfusion** — use of a sorbent cartridge or column to remove certain agents from the blood. Examples of hemoperfusion devices include: PMX (also known as Toraymyxin), CytoSorb, Jafron HA380, and the D2000 Adsorption Cartridge.
- **Hemofiltration** — use of an adsorptive filtering membrane to remove inflammatory mediators. An example of a hemofiltration membrane device is oXiris (an AN69 membrane)

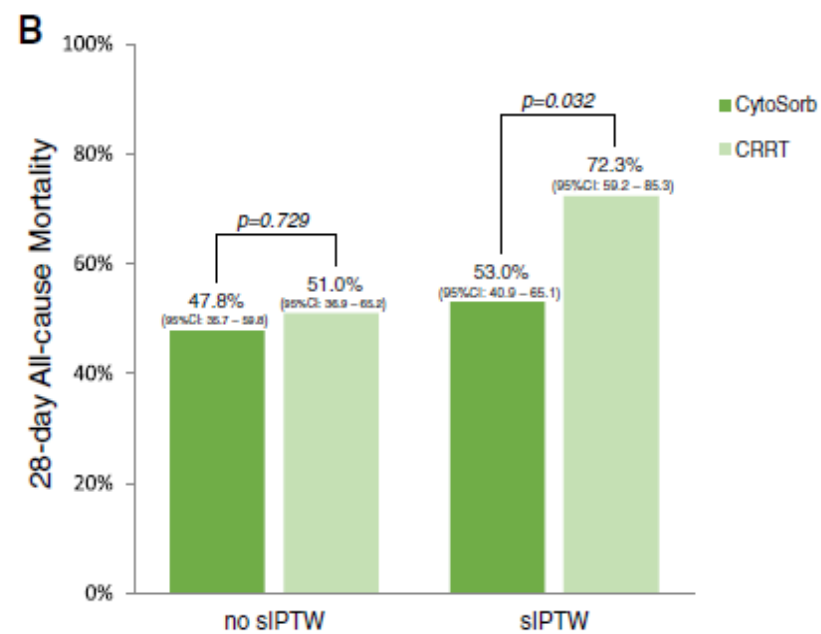
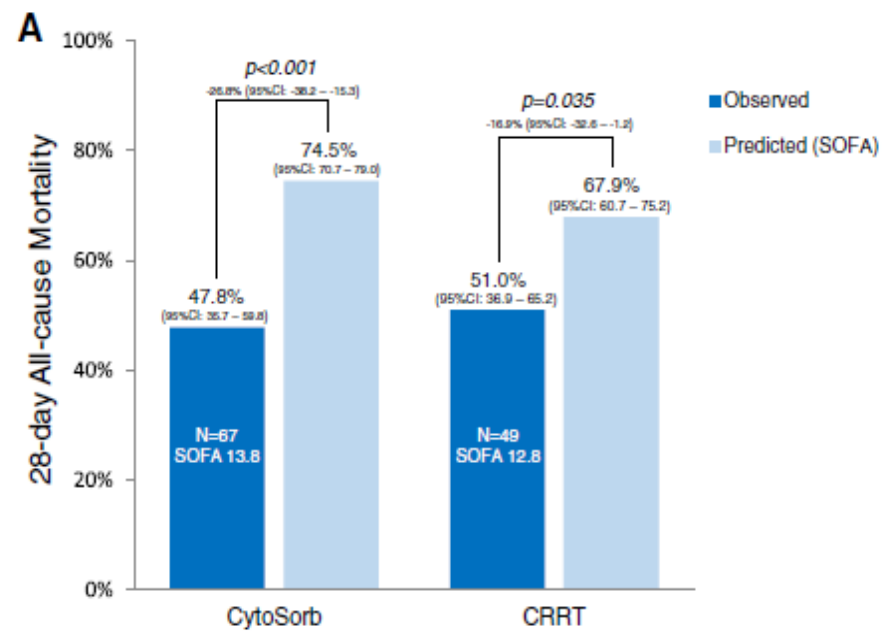
RESEARCH

Open Access

# Hemoadsorption with CytoSorb shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study



Willem Pieter Brouwer<sup>1,2\*</sup> , Servet Duran<sup>3</sup>, Martijn Kuijper<sup>4</sup> and Can Ince<sup>5</sup>



**Fig. 2 a** Observed versus predicted mortality rate according to the SOFA score for CytoSorb- and CRRT-treated patients. **b** CytoSorb is associated with a reduced 28-day mortality in sIPTW analysis

- The nonspecific or specific removal of some damage-associated molecular patterns and/or pathogen-associated molecular patterns most likely plays a key role in the modulation of the inflammatory response to sepsis.
- The removal result in a decrease of peaks of cytokine concentrations and/ or a modification of the cytokine/chemokine ratio from the tissues to the blood, positively impacting the leukocyte trafficking.
- The leading cause of these complications is usually cytokine storms, which contribute to a significant systemic inflammatory reaction, leading to damage in the organs including the lung, heart, and kidney.












RESEARCH ARTICLE

Open Access

# Effectiveness of extracorporeal blood purification (hemoadsorption) in patients with severe coronavirus disease 2019 (COVID-19)



Masoumeh Asgharpour<sup>1</sup> , Hamed Mehdinezhad<sup>1</sup> , Masoumeh Bayani<sup>2</sup> ,  
Mahmoud Sadeghi Haddad Zavareh<sup>2</sup> , Seyed Hossein Hamidi<sup>3</sup> , Roghayeh Akbari<sup>4</sup> , Reza Ghadimi<sup>5</sup> ,  
Ali Bijani<sup>5</sup>  and Simin Mouodi<sup>5\*</sup> 

**Conclusions:** Extracorporeal hemoadsorption could improve the general condition in most of recruited patients with severe coronavirus disease; however, large prospective multicenter trials in carefully selected patients are needed to definitely evaluate the efficacy of hemoperfusion in COVID-19 patients.

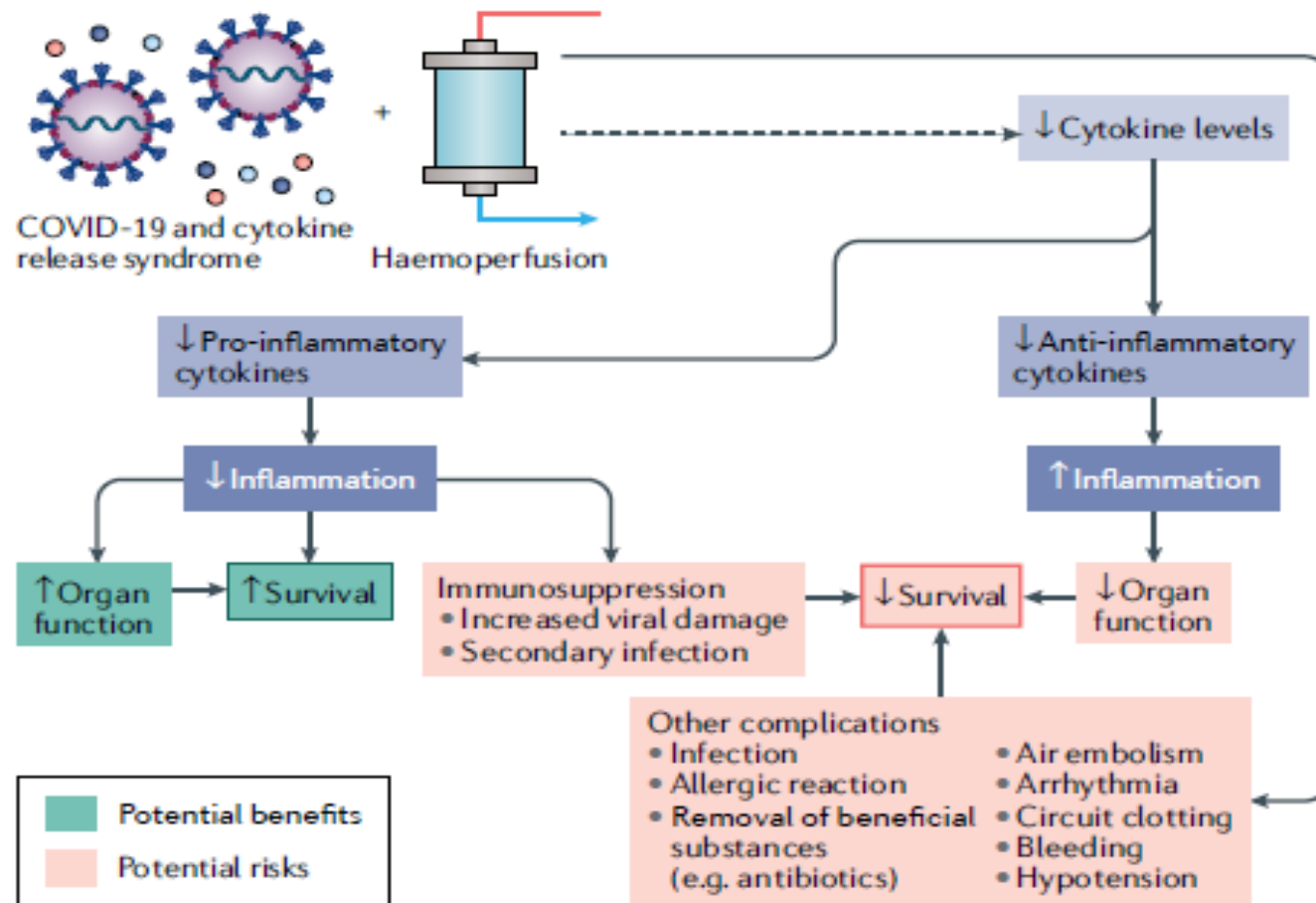
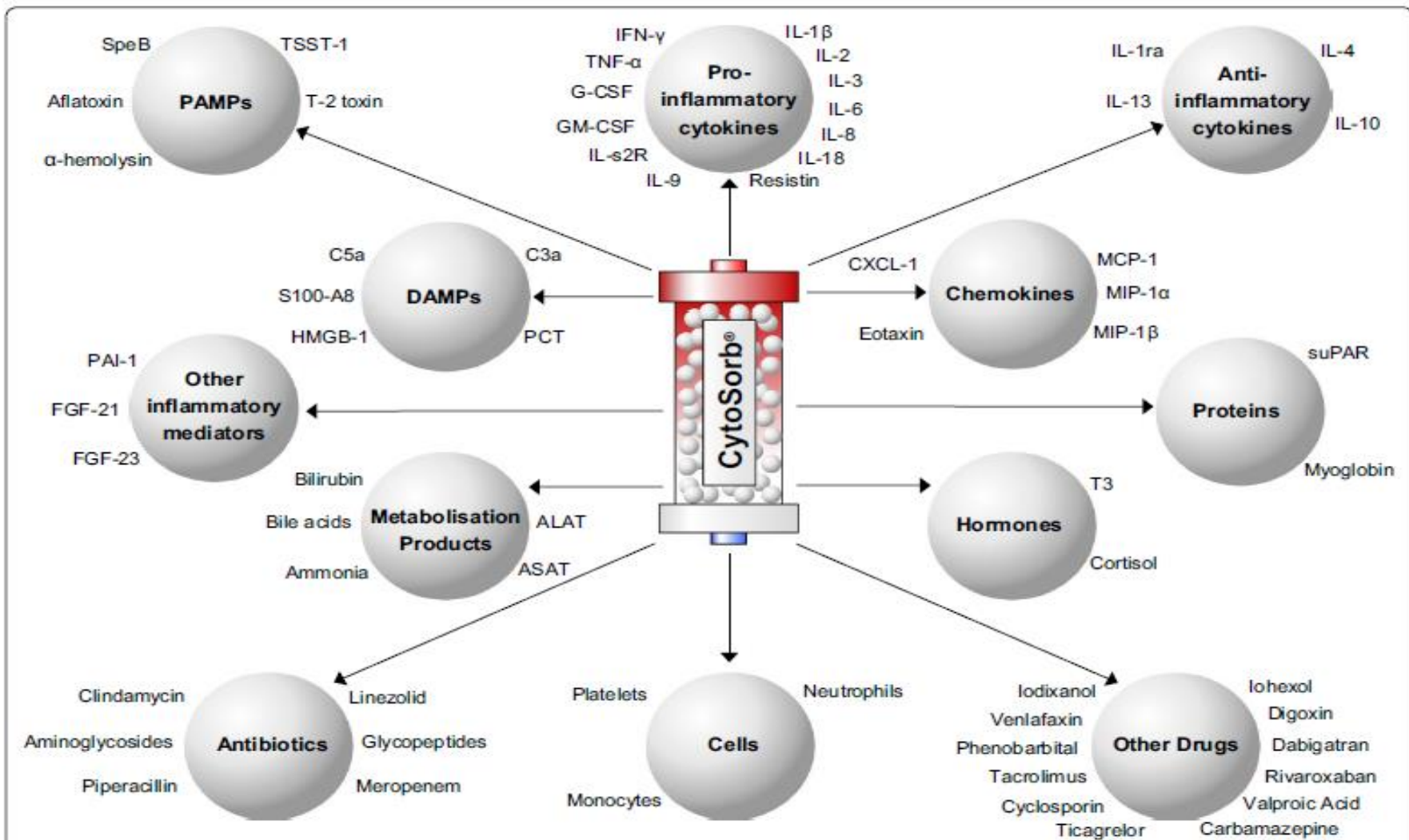


Fig. 1 | Potential risks and benefits of haemoperfusion for cytokine removal in severe COVID-19. Although haemoperfusion can remove cytokines from the blood, evidence suggests that this intervention might not substantially reduce circulating cytokine levels<sup>6</sup>. Moreover, in addition to potential benefits, a non-selective reduction in pro-inflammatory and anti-inflammatory cytokines carries potential risks. Haemoperfusion can also potentially lead to complications that are not directly related to cytokine removal, including hypotension and arrhythmias.

- The **CytoSorb** cartridge is filled with biocompatible polymer beads about the size of grains of salt. The pores in each bead are sized to allow larger components, such as blood cells, to pass around the beads and smaller components, such as electrolytes, to pass through.
- However, hydrophobic substances, such as cytokines, are trapped inside the beads and removed from the bloodstream.
- An initial three-day-course of therapy for patients with severe COVID-19, with a cartridge change every 12 hours on day one and every 24 hours on days two and three.
- After the third day of treatment, patients should be assessed to determine whether there are signs of benefit, in which case CytoSorb treatment can continue until their conditions are stable.

- The **Jafron** adsorption cartridge consists of a “neutral, macroporous resin,” with a large surface area that adsorbs inflammatory agents, including cytokines.
- The Jafron hemoperfusion cartridges recommend a three-day-course of therapy, with two treatments (cartridges) in the first 24 hours and one treatment on days two and three





**Fig. 1** Scope of adsorption by CytoSorb®. Figure mostly based on in vitro data. The clinical relevance of CytoSorb® hemoadsorption for the majority of those molecules remains to be evaluated. DAMPs damage-associated molecular patterns, FGF fibroblast growth factor, HMGB-1 high-mobility group box 1, MCP-1 monocyte chemoattractant protein 1, MIP macrophage inflammatory protein, PAI-1 plasminogen activator-inhibitor 1, PAMPs pathogen-associated molecular patterns, PCT procalcitonin, SpeB streptococcal pyrogenic exotoxin B, S100-A8 S100 calcium-binding protein A8, suPAR soluble urokinase-type plasminogen activator receptor, T3 triiodothyronine, TSST-1 toxic shock syndrome toxin 1

# Indications

- IL6 > 400-1000 pg/ml
- Ferritin > 1000-1500
- Lactate > 4 (better response in lact > 6)
- CRP > 125
- CPK > 2 times NL value
- Vasoplegic shock with NE > 0.3 micr/kg/min
- MOF

# Contraindication

## Absolute

- Thrombocytopenia < 20000
- Pregnancy
- Allergy
- SCA
- Skill

## Relative

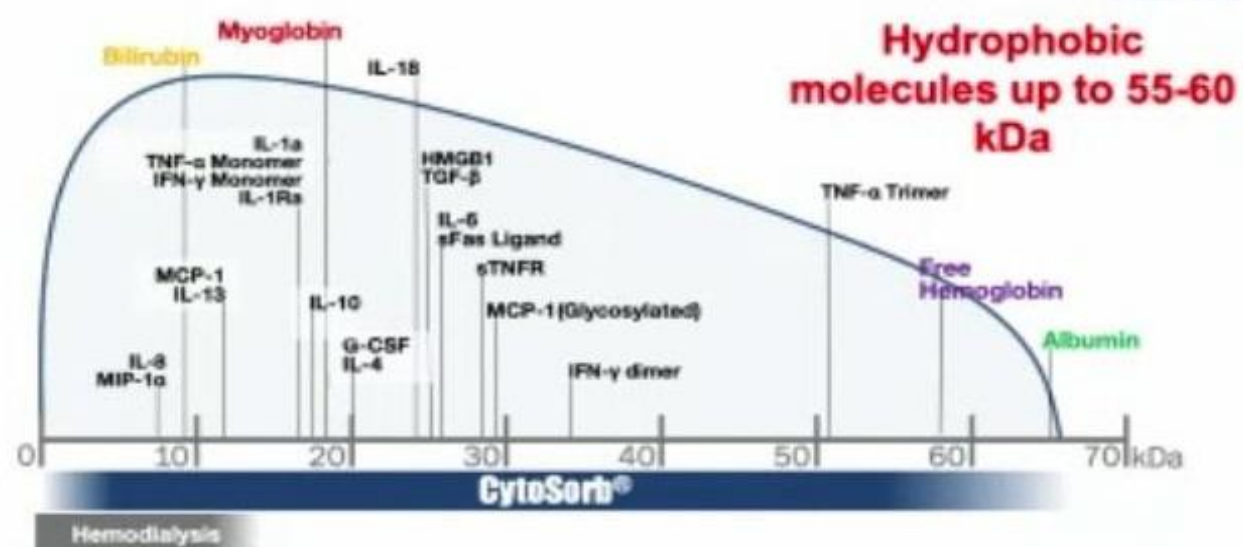
- BMI > 40
- HIT
- Age < 12

# Key points

- Time(onset: ASAP, duration: 3-7 d, exchange filter /24h)
  - Phenotype(polymorphism)
  - Severity(Ref Septic shock, SOFA)
  - Biomarkers: bed side(CRP,IL6)
- 
- 1980s: Kt/v
  - 2000s: adequacy of dialysis
  - 2020: adequacy of adsorbent(sufficient, appropriate, high)



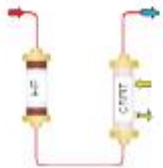
## Removal selectivity: Role of size exclusion



a



b



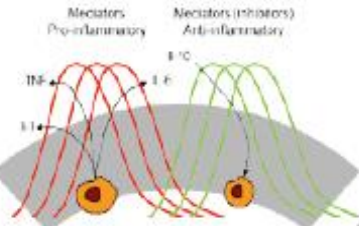
**Cytokine Removal**

- Hemoadsorption
- Hemofiltration - CVWH
- High dose CVWH

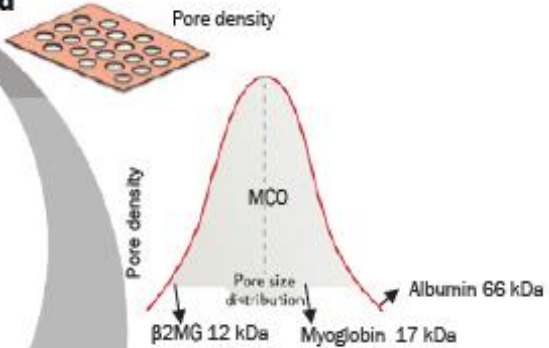
c

**Cytokines**

- Cytokine release syndrome
- Mechanical ventilation
- ECMO
- CRRT circuit
- Hemophagocytic syndrome



d



**Cytokine Removal**

- HCO membrane
- MCO membrane

e

**Crosstalk Interventions**

- Cardiomyopathy  $\rightarrow$  LVAD; AV ECMO
- Peak airway pressure + IAH  $\rightarrow$  VV ECMO, ECCO<sub>2</sub>R, CRRT
- Rhabdomyolysis  $\rightarrow$  CRRT, HCO or MCO membranes



**Crosstalk**

- Cardiomyopathy  $\rightarrow$  Cardiorenal syndrome type 1
- Alveolar damage  $\rightarrow$  Renal medullary hypoxia
- Peak airway pressure + IAH  $\rightarrow$  Renal compartment syndrome
- Rhabdomyolysis  $\rightarrow$  Tubular toxicity



COVID-19

f

**Systemic Interventions**

- Positive Fluid Balance  $\rightarrow$  Continuous ultrafiltration + Diuretics
- Endothelial damage + Third space fluid loss + Hypotension  $\rightarrow$  Vasopressors + Fluid expansion
- Nephrotic syndrome
- Metabolic acidosis
- Hyperkalemia  $\rightarrow$  CRRT

**Systemic**

- Positive Fluid Balance  $\rightarrow$  Renal compartment syndrome
- Endothelial damage + Third space fluid loss + Hypotension  $\rightarrow$  Renal hypoperfusion
- Nephrotic syndrome
- Metabolic acidosis
- Hyperkalemia




- Blood flows above 150 mL/min and the use of diffusive techniques (CVVHD) with minimal FF(25%) further help avoiding circuit clotting.
- In long-term treatment, regional citrate anticoagulation, (although no evidence of superior outcomes has been provided).
- Hemoadsorption would essentially reduce high levels of several mediators and by this 'limit the storm' in cytokine storm syndrome, rather than actively targeting individual pathways during inflammation.

RESEARCH

Open Access

# Blood purification therapy with a hemodiafilter featuring enhanced adsorptive properties for cytokine removal in patients presenting COVID-19: a pilot study



Gianluca Villa<sup>1,2\*</sup> , Stefano Romagnoli<sup>1,2</sup>, Silvia De Rosa<sup>3,4</sup>, Massimiliano Greco<sup>5,6</sup>, Marco Resta<sup>7</sup>, Diego Pomarè Montin<sup>1,4</sup>, Federico Prato<sup>8</sup>, Francesco Patera<sup>9</sup>, Fiorenza Ferrari<sup>4,10</sup>, Giuseppe Rotondo<sup>11</sup> and Claudio Ronco<sup>4,12,13</sup>

Compared to the expected mortality rates, the mean observed rates were 8.3% lower after treatment.

The best improvement in mortality rate was observed in patients receiving EBP early on during the ICU stay.

an observational study

37 patients with AKI

oXiris membrane

## Measures to improve circuit life

### Anticoagulants

**Maintain patency  
of extracorporeal  
circuit**

- Avoid minor clotting in the capillary fibers and reduced solute clearances
- Avoid major clotting leading to loss of the filter, tubing, and blood in the circuit

**Avoid bleeding**

- Avoid patient's complications

**Provide an inert  
surface-blood  
interaction**

- Minimize activation of complement and cytokine cascade
- Reduce cellular activation

**Maintaining the extracorporeal circuit is crucial for delivering the treatment effectively**



## Measures to improve circuit life Non-anticoagulant

### Reducing stasis of flow

- Vascular access (dimensions, material, tip position, vein choice)
- Training (reaction time to alarm, recognition of kinking catheter, etc)

### Optimizing setting

- Filtration fraction
- Predilution vs postdilution
- Clogging
- Membranes
- Filter size


Maintaining the extracorporeal circuit is crucial for delivering the treatment effectively

# Anticoagulation free

- High risk of bleeding
  - Liver dysfunction
  - Coagulation disorders
- 
- Sites of clot formation
- Hemofilter
- Bubble trap, deaeration chamber
- Catheter
- Leurlock and 3 way stopcock connections

# Cytoscore: >8

a new tool to optimize the starting point

**CytoScore ECSISS** 

	0 Points	1 Point	2 Points	
Lactate mmol/l	< 2.0		≥ 2.0	
Lactate change / 6hrs	↓ decreased	↑ ≤ 50%	↑ > 50%	
NE µg/kg/min (MAP=65)	< 0.1		≥ 0.1	
NE change / 6hrs	↓ decreased	↑ ≤ 50%	↑ > 50%	
2 <sup>nd</sup> catecholamine / vasopressor	No	Yes		
Hydrocortisone use	No	Yes		
Volume bolus 30 ml/kgbw	No	< 2 boli	≥ 2 boli	
			<b>Total</b>	

7<sup>th</sup> International CytoSorb Users' Meeting | Virtual | Live from Berlin, Germany | Oct 29, 2020

- Clinical data suggest high degree of patient safety
- No relevant removal of coagulation factors
- Relevant removal of various drugs
- Removal primarily in early phase of HP(15-60min)
- Sufficiently high dosage and TDM advisable.

---

# Hemoperfusion as a Potential Treatment for Critically Ill COVID-19 Patients with Cytokine Storm

Kamran Shadvar<sup>a</sup> Ali Tagizadiyeh<sup>b</sup> Ali Akbar Gamari<sup>a</sup> Hassan Soleimanpour<sup>c</sup>  
Ata Mahmoodpoor<sup>a</sup>

<sup>a</sup>Department of Anesthesiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran;

<sup>b</sup>Tuberculosis and Lung Research Center, Tabriz University of Medical Sciences, Tabriz, Iran; <sup>c</sup>Department of Emergency Medicine, Medicine, Faculty of Medicine, Tabriz University of Medical sciences, Tabriz, Iran

- Finally, our results showed that hemoperfusion can decrease the level of inflammation and organ dysfunction in critically ill patients with COVID-19. We need more studies to show the best time for implementation of hemoperfusion and number of its sessions in outcome of these patients.
- Moreover, all ICU staff and physicians should be familiar with the concept of hemoperfusion in management of critically ill patients.
- So, hemoperfusion (early application) combined with appropriate antiviral therapies and supportive therapy may be considered as an adjunctive treatment for critically ill COVID-19 patients.
- For the moment, the pathophysiological rationale is the only reason to recommend that application of hemoperfusion, and a personalized evaluation is advised. In addition, if such intervention is being considered, it seems logical to apply it as soon as possible.



- According to current experience and in the absence of any specific therapy besides supportive measures, cytokine removal strategies should be reserved for COVID-19 patients with evidence of high circulating cytokines such as IL-6 and IL-8, a biochemically determined inflammatory status, high SOFA score, clinical symptoms of hemodynamic instability requiring vasopressors, and initial signs of immune dysregulation or disorders of coagulation cascade.
- Markers such as plasma ferritin or urinary biomarkers of kidney stress may also be useful to identify cases of hyper-inflammation.
- Clinical criteria alone may be surrogates of hyper-inflammation, but they should be evaluated case by case.

- In the future, genetic profiling may guide the initiation of this therapeutic strategy for specific patients.
- Due to frequent mobilization and pronation, patients may be treated with prolonged intermitted sessions (PIRRT) to allow nursing maneuvers.
- Because of severe hemodynamic instability and the need to control the patients' fluid balance, fluid removal should be carefully scheduled to avoid hypotension that could worsen kidney injury or delay recovery.

- These therapies, although considered as “under scientific investigation,” “salvage,” or “compassionate use” interventions, still represent an option for severe CRS and, in particular, for COVID-19 patients where pharmacological alternatives are lacking.
- For the moment, the pathophysiological rationale is the only reason to suggest the application of these methods, and a case-by-case evaluation is advised, although if such treatments are being considered, it seems logical to apply them early.

LETTER

Open Access

CytoResc – “CytoSorb” Rescue for critically ill patients undergoing the COVID-19 Cytokine Storm: A structured summary of a study protocol for a randomized controlled trial



# Study protocol

- CRP > 100 mg/l
- PCT < 0.2 ng/l
- Cytokine storm (vasoplegic shock: NE > 0.2 micro/kg/min)
  
- 3-7 days
- Catheter exchange every 24 hours
  
- P.outcome: resolution of vasoplegic shock
- S.outcome: mortality at 7 and 28 day, IL6, MV, ICU stay, catecholamine dose, AKI

# CYTOCOV-19

CytoSorb® in COVID-19-sCAP  
- single-centre RCT -

**Question:**

Does the reduction of elevated cytokine levels by hemadsorption have a positive effect on the disease severity of sCAP patients with COVID-19 and shock in terms of sustained hemodynamic stabilization?

**Inclusion criteria:**

- Confirmed COVID 19
- Refractory shock: MAP  $\leq$  65 mmHg with vasopressor therapy and adequate fluid substitution
- Noradrenaline dose  $\geq$  0.2  $\mu$ g/kg/min
- IL-6  $\geq$  500 ng/l
- Indication for extracorporeal therapy (e.g.: CRRT or ECMO, ECCO<sub>2</sub>R)
- Age  $\geq$  18 and  $\leq$  90 y

**Exclusion criteria:**

- Liver cirrhosis Child-Pugh C
- Standing DNR-order, moribund patient
- Expected survival due to comorbidities  $\leq$  14 d
- Pregnancy oder lactation
- Participation in interventional trial

**Primary endpoint:**

- Significant stabilisation of hemodynamics („shock reversal“), defined as reduction of noradrenaline requirements ( $\leq$  0.05  $\mu$ g/kg/min) to maintain MAP  $\geq$  65 mmHg for at least 24 h compared to controls



# Cytosorb registry

- Data from interim analysis:
- Severe sepsis/MOF

Haemoperfusion should only be used for COVID-19 in the context of randomized trials

**! DANGER**



OUTBREAK ALERT  
CORONA VIRUS

**#COVID19**