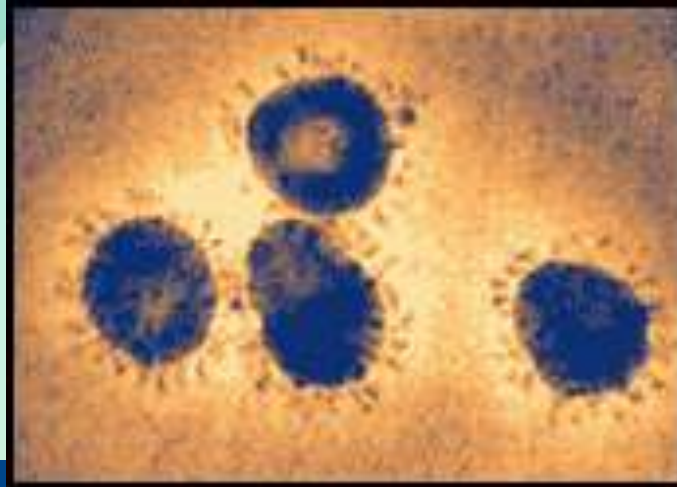


Infection Control in Dialysis Facilities in the Age of Coronavirus



Alan S. Kliger, MD
April 2021



ALAN S. KLIGER, MD



NTDS Project Chair; COVID-19 Response Team Co-Chair

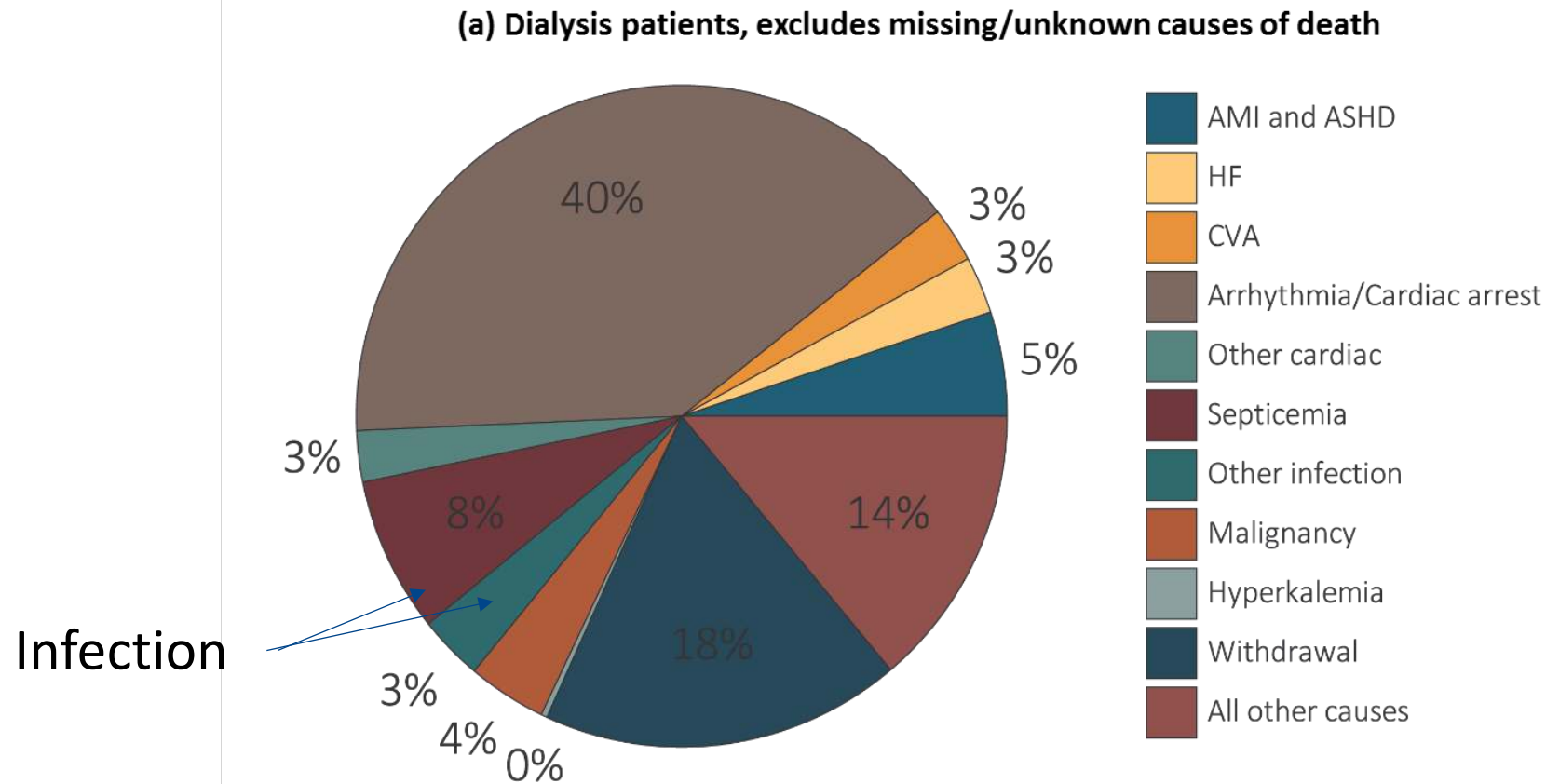
Yale School of Medicine

- **Consultancy Agreements:** ASN; National Institutes of Diabetes, Digestive Diseases and the Kidney
- **Honoraria:** several universities and medical schools, professional organizations - honoraria for lectures, seminars, webinars;
- **Scientific Advisor or Membership:** Qualidigm (Quality Improvement Organization);
- **Other Interests/Relationships:** Renal Physicians Association; American Society of Nephrology

**An epidemiologist,
an ICU doctor and
a scientist walk
into a bar...**

**Just kidding, they
know better.**

vol 2 Figure 5.4 Unadjusted percentages of deaths in 2015 by cause, with and without missing data, by modality among dialysis patients and transplant recipients

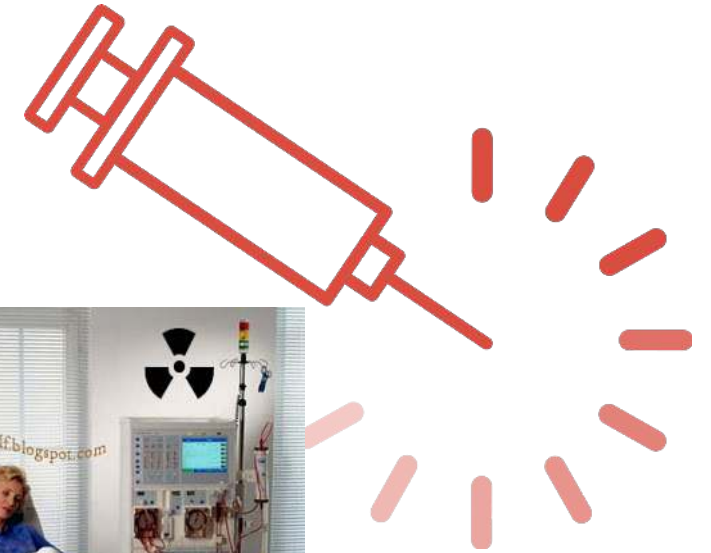


Data Source: Special analysis using Reference Table H.12_Dialysis and H.12_Tx. Mortality among 2015 prevalent patients. (a) Dialysis patients, denominator excludes missing/unknown causes of death. (b) Transplant recipients, denominator excludes missing/unknown causes of death. (c) Dialysis patients, denominator includes missing/unknown causes of death. (d) Transplant recipients, denominator includes missing/unknown causes of death. Abbreviations: AMI, acute myocardial infarction; ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CVA, cerebrovascular accident.



CDC Studies: Major Risk Areas for Infection

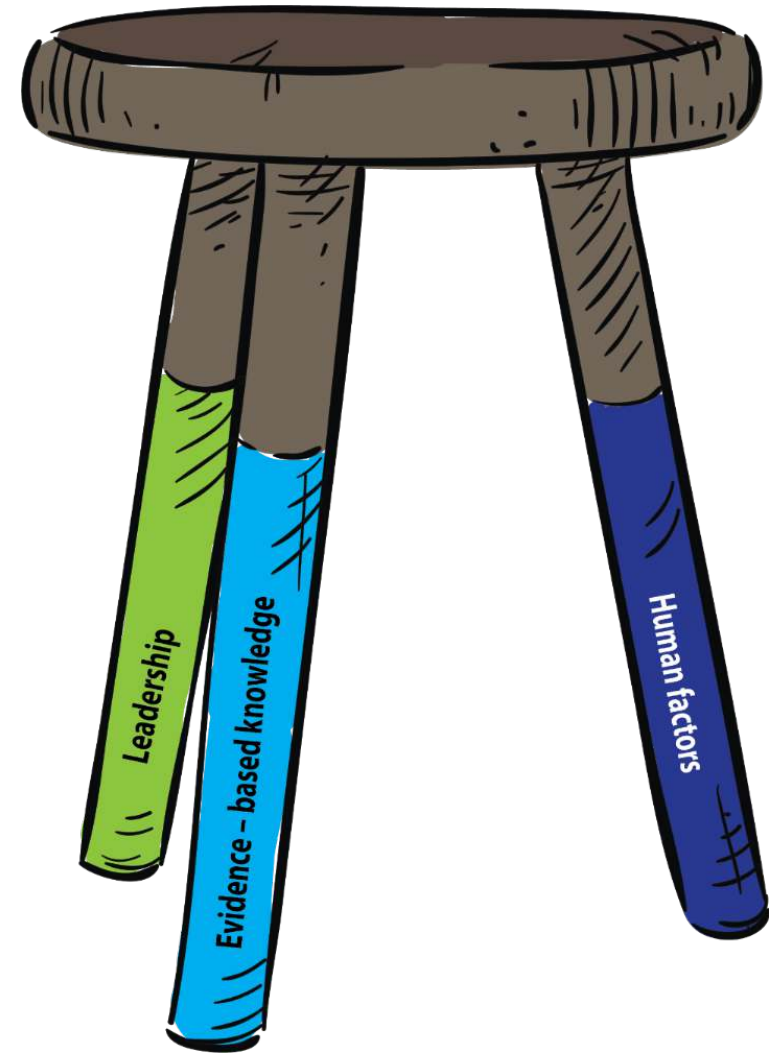
- Hand Hygiene
- Catheter Use
- Injection Safety
- Station Disinfection





NTDS Dialysis Quality and Safety Platform

- **Identify, Develop, Share Evidence-Based Knowledge:**
 - Foster learning: staff and patients
 - Educational conferences & webinars
 - www.asn-online.org/NTDS
- **Improve System Function Using Human Factors Engineering**
 - Measure and improve the way care is delivered in dialysis facilities
- **Promote Effective Leadership**
 - Power of Inspirational Leadership
 - Commit to eliminate infections
 - Create psychological safety and empower others
 - Nephrologists must lead by example





Dialysis Care Checklist Pilot

- Goal: Determine feasibility of increasing the use of CDC chairside checklists to improve infection control practices in outpatient dialysis.
- Pilot study results in preparation

The screenshot shows a digital form titled "Dialysis Care Checklist". It includes two required sections: "Who is observing the procedure?" with radio button options for Technician, Nurse, Social Worker, Dietician, and Physician; and "Procedure" with radio button options for Catheter Connection, Catheter Disconnection, and Catheter Exit Site Care. A "NEXT" button is at the bottom of the form. Overlaid on the bottom right is a summary box for "2. Hand hygiene performed" based on 9 responses. It features a pie chart with a blue slice representing 77.8% (Yes) and a red slice representing 22.2% (No). A legend to the right of the chart identifies blue as "Yes" and red as "No".

Response	Percentage
Yes	77.8%
No	22.2%



Blood Culture Standardization

- A set of standard Recommendations (12) and Rationale for each Recommendation based on the literature and guidance from professional organizations (CDC, IDSA, CLSI)
- Includes 2 sites from which blood can be accessed, including the catheter hub, the hemodialysis circuit (tubing connected to the catheter hub), and a peripheral vein
- SBAR introductory slide set and template
- A step-by-step blood culture draw procedure
- A competency checklist and recommendations
- https://www.asn-online.org/g/blast/files/NTDS_Blood_Culture_Collection_Standardization_combined_01.16.2020.pdf

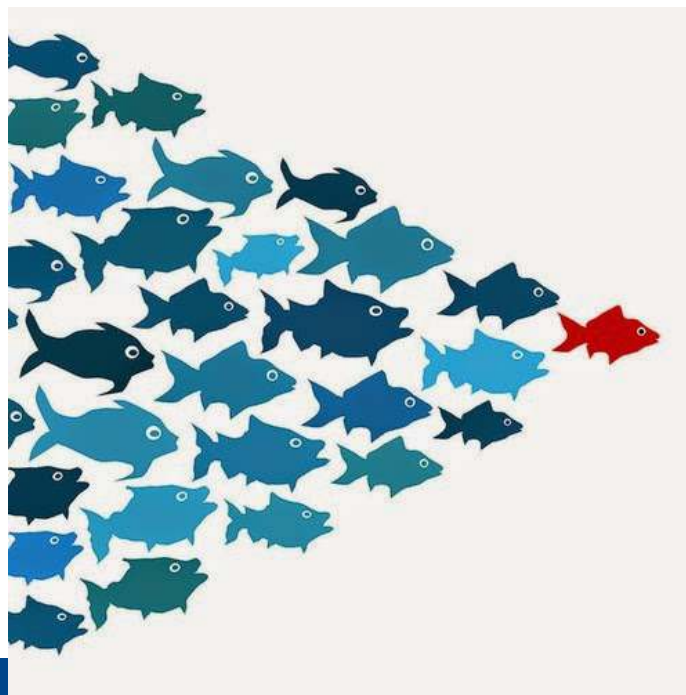


Standardization of Blood Culture Collection for Patients Receiving In-Center Hemodialysis

January 16, 2020
Submitted by
The American Society of Nephrology (ASN)
1401 H Street NW
Suite 90
Washington, DC 20004



Developing Effective Leadership and Culture in Dialysis






Leadership, Education and Culture Change

- Kidney Leadership Academy (Pilot with NKC)
 - Agenda
 - Personality Types
 - Team Verses Group
 - Leading Your Way to Success: Five Key Leadership Lessons
 - Essence of Change: Effective Strategies for Change Management
 - Application of Effective Conflict Management for Physicians
 - Competing Stakeholders for Dialysis
 - Six-month Follow-up
 - Evaluation




A large orange circle is positioned on the left side of the slide, partially cut off by the edge.

Human Factors Engineering

Human factors is a scientific discipline that examines human capabilities and limitations and applies that knowledge to the design of tools, technology, and processes to facilitate safe, efficient, and effective work.

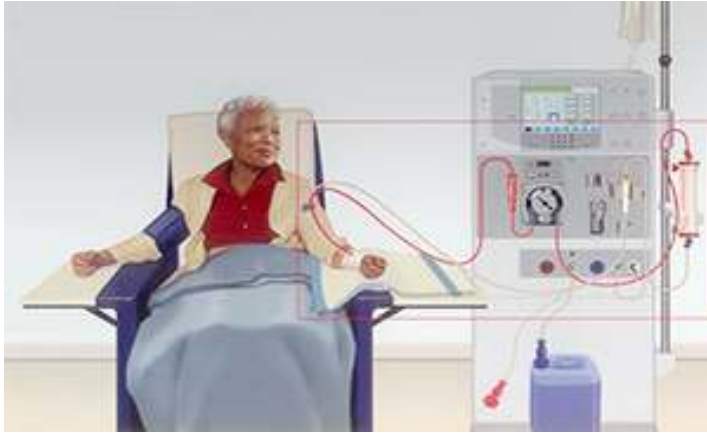
The focus of human factors is to integrate the scientific findings from psychology and engineering on human performance and to apply those findings to the design of daily work.

A series of green dashed line segments are arranged in a curved, upward-sloping pattern in the bottom right corner of the slide.

**We can't change the human
condition, but we can change the
conditions in which humans work**



Work as Imagined

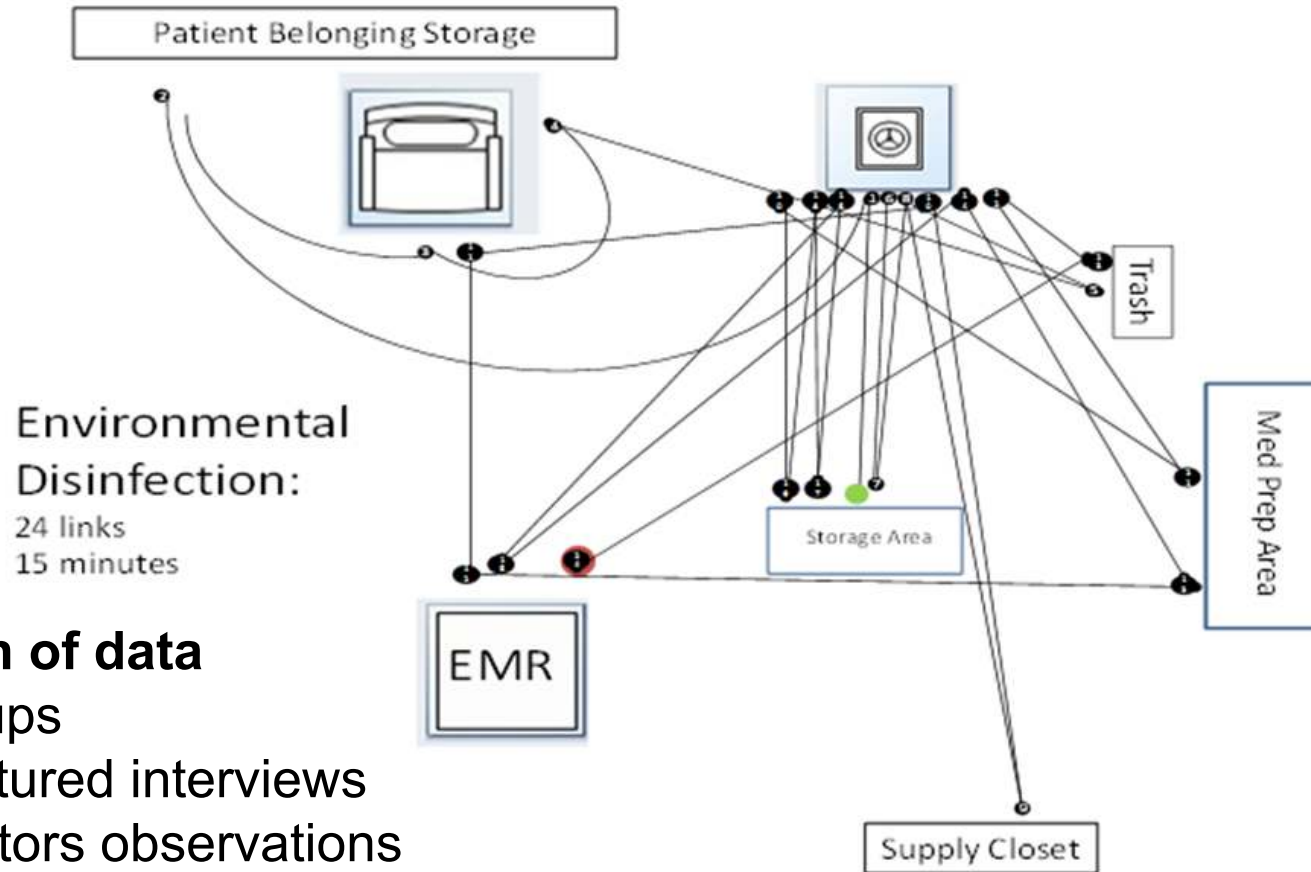


Work as performed





Human Factors Assessment: Methods



Link analysis created while observing disinfection of the dialysis station.

Triangulation of data

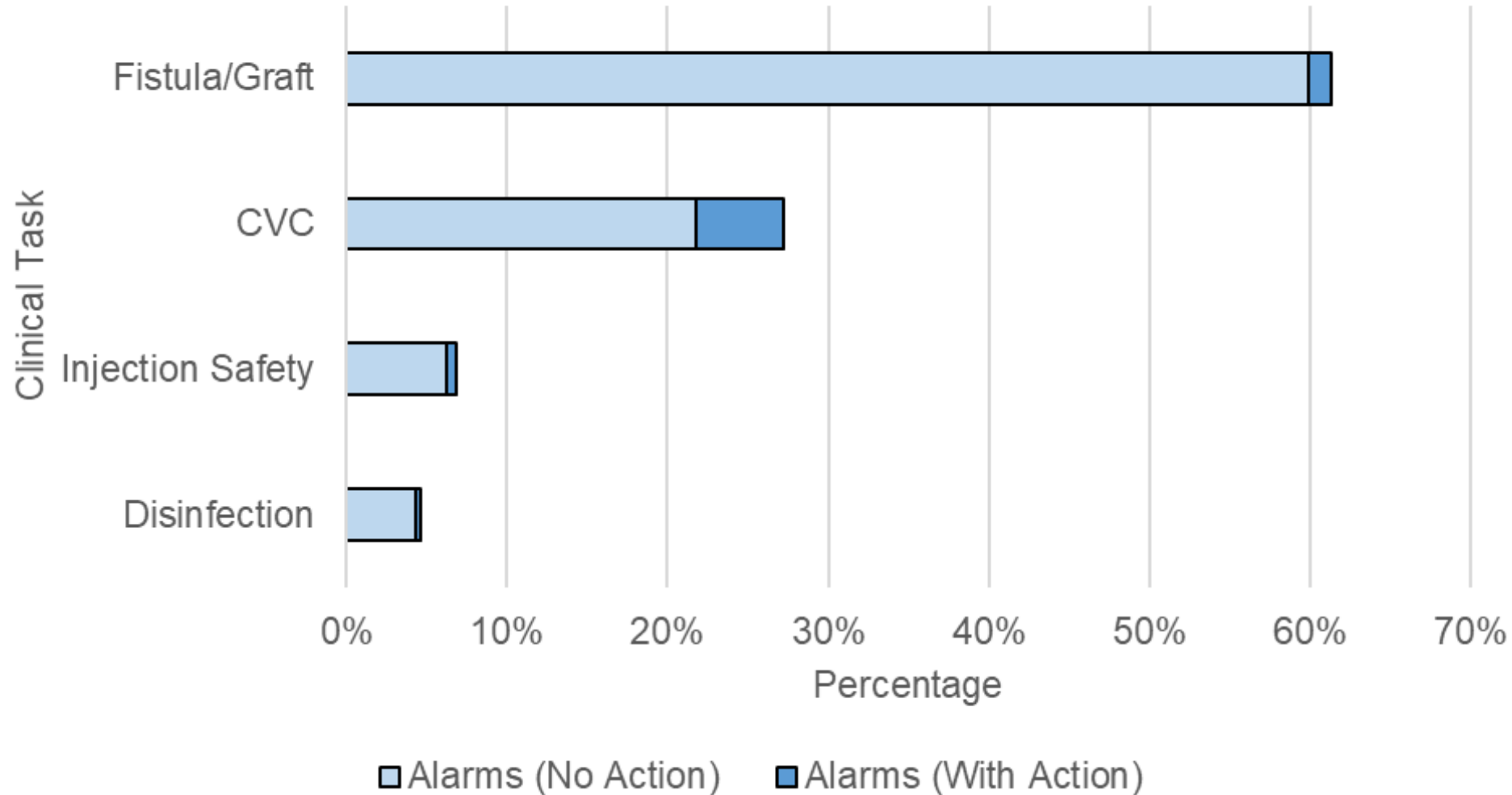
- Focus groups
- Semi-structured interviews
- Human factors observations
 - TimeCat
 - Link analyses
 - Ethnographic observations
- Infection Prevention observations



TimeCat used to capture and organize data

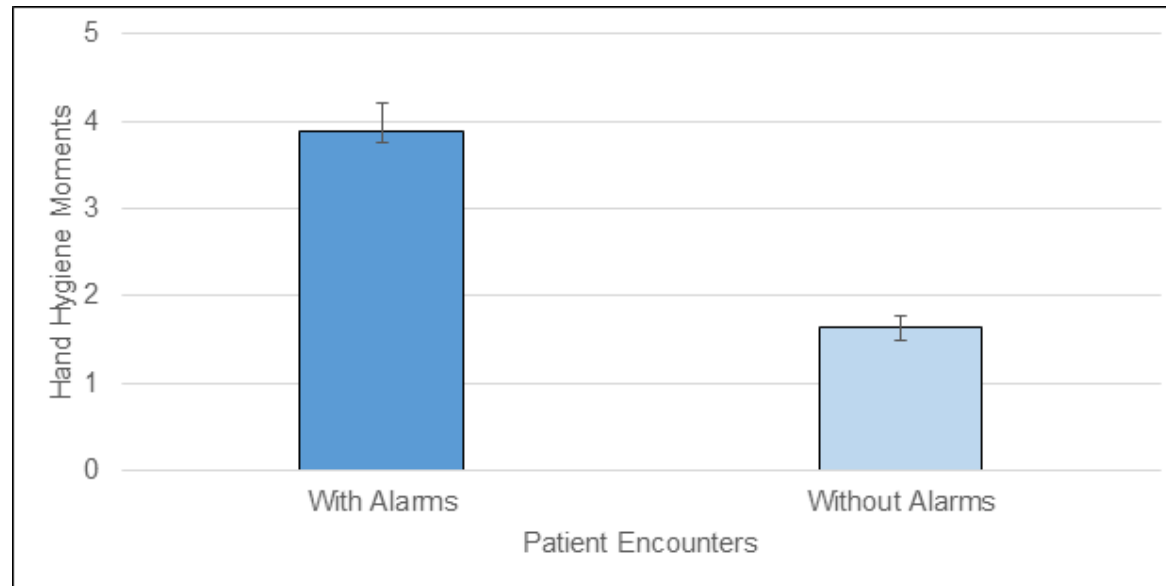


Alarms During Critical Tasks





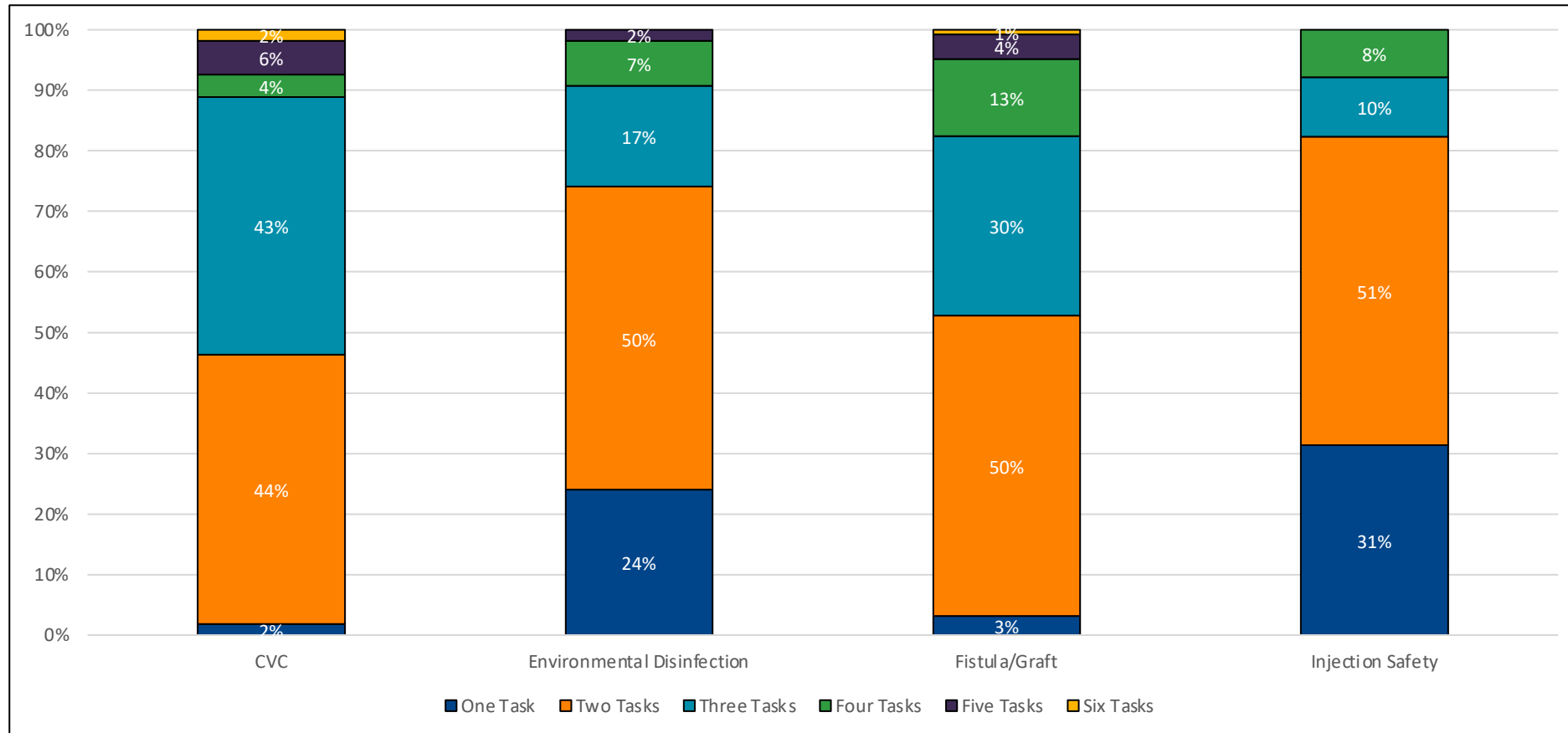
Alarms increase the need for hand hygiene and are often NOT matched to work-flow



Machines are designed to be touched (touch screen). BUT every touch requires hand hygiene and increases the risk for skipped-steps

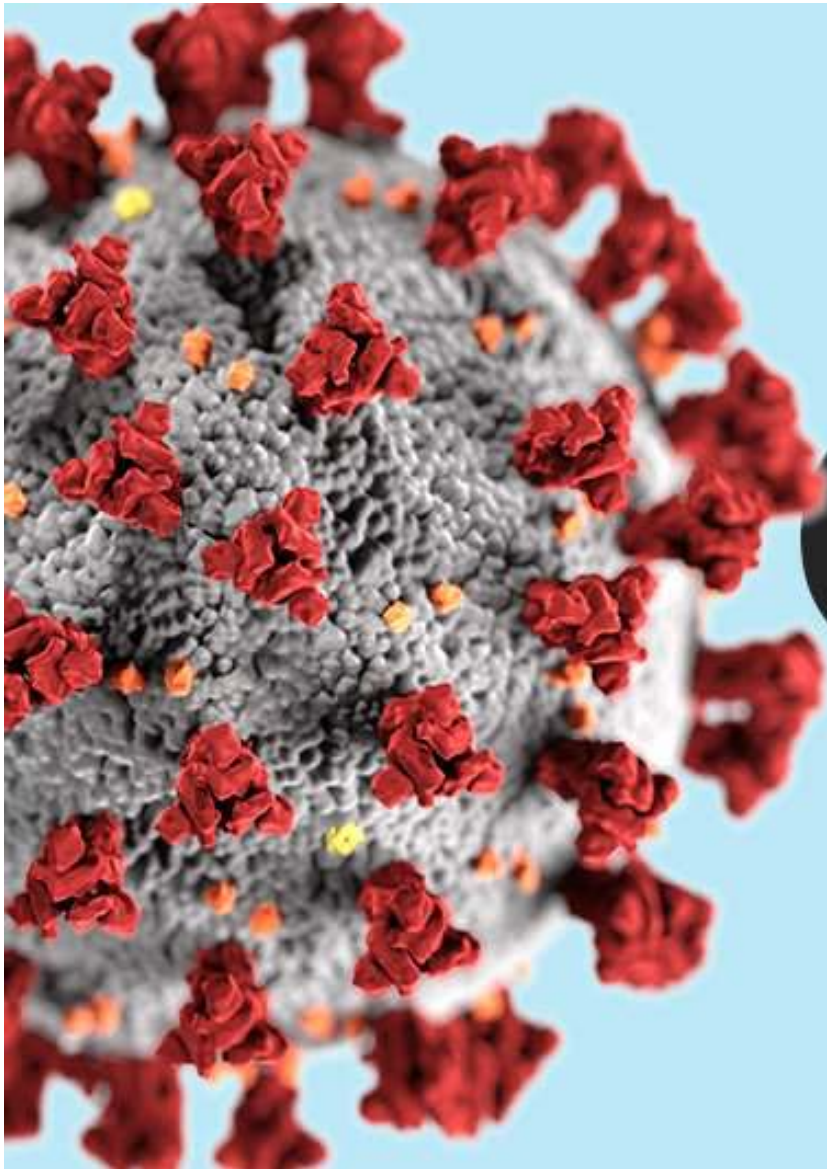


Task-Stacking and Task-Switching are Common



- 72.9% of the time 2 or more tasks are done simultaneously, and half the time 2 tasks are being completed at once.

Infection Control in the Age of Coronavirus



COVID-19
CORONAVIRUS PANDEMIC



Dialysis Patients are at Higher Risk of Acquiring COVID-19

- Co-Morbidities: Diabetes, Obesity, BP, CVD
- Frailty
- Age
- Immune Status
- In-Center
 - Cannot Social Distance: frequent exposure to staff and patients
 - Transportation



Hemodialysis Transportation

- 2013 USRDS



- Private cars (drove themselves) 25.3%



- Public transportation (bus/metro/taxi) – 7.9 %



- Help from others (van, ambulance etc) – 66.8%



West London Dialysis

Corbett et al, JASN 2020 August 31 (8):1815

- 1,530 dialysis patients
- 300 developed COVID-19 (19.6%)
- More likely among in-center than home dialysis patients
- Clustering in specific dialysis units and shifts
- High rates of nursing staff illness
- Modeling suggested that measures implemented reduced transmission

28-day case fatality rate Dialysis patients

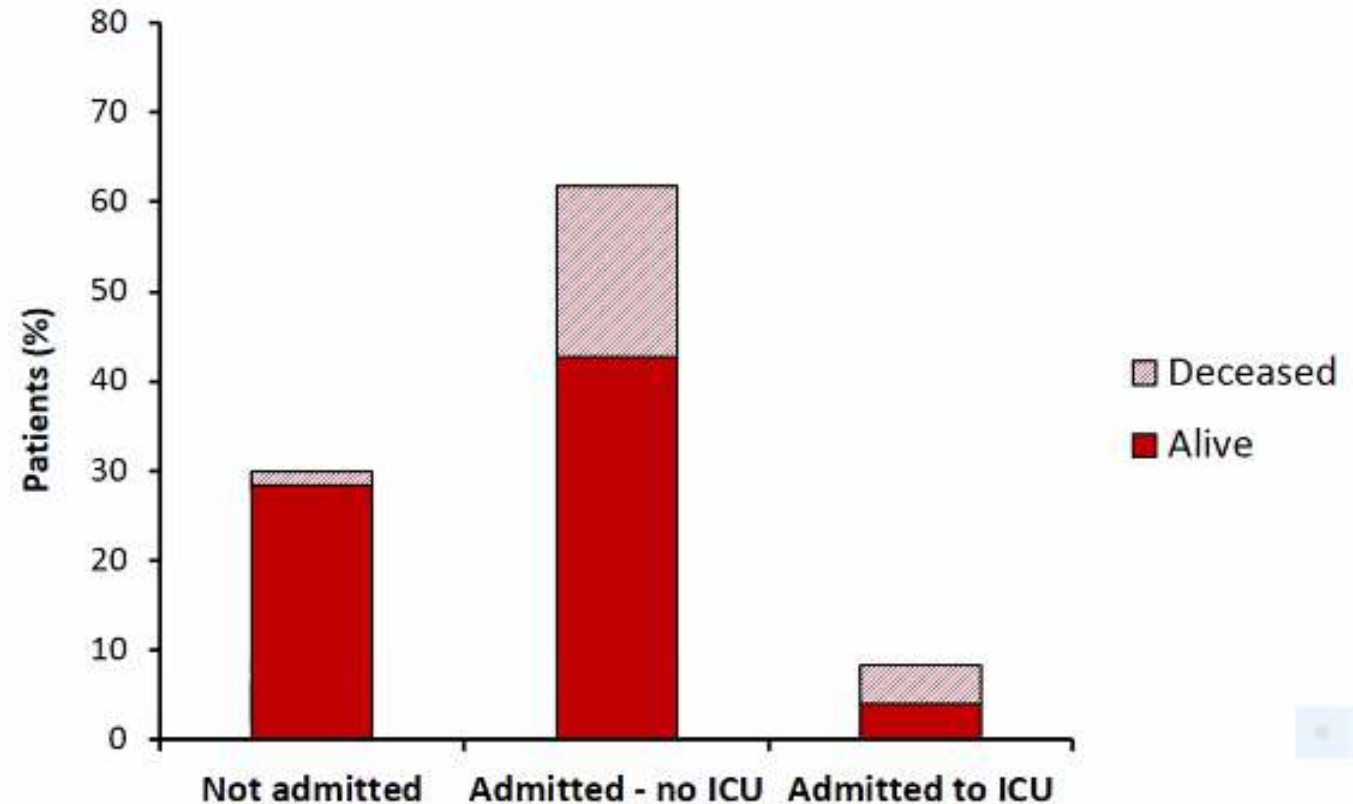
All patients: 25%

Not admitted patients: 5%

Hospitalized patients: 33%

Patients admitted to ICU: 53%

Survival according to admission status

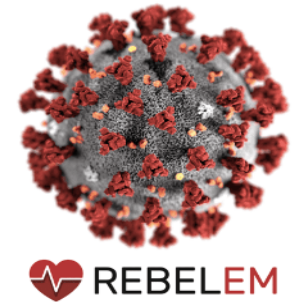




Lessons Learned: Outpatient Dialysis

- Come to dialysis
- Call in ahead of your treatment if you are have fever, cough, etc.
- Protect yourself at home: face covering, social distancing, hand washing
- If you are sick: don't just tough it out at home: call your doctor. Come to hospital
- Hemodialysis facility lessons
 - Transportation: anticipate and educate
 - Segregate proven COVID-19 and PUI
 - Screen patients and staff every shift: questions, temp
 - No waiting rooms
 - Mental health resources
 - Prepare for the long haul (staff shortages, staff health, PPE)

COVID-19: Screening, Testing, PUI, and Returning to Work



[This Photo](#) by Unknown Author is licensed under [CC BY-NC-ND](#)

Reporting PPE Shortages

- If your facility is concerned about a potential or imminent shortage of PPE, alert your state/local health department and local healthcare coalition, as they are best positioned to help facilities troubleshoot through temporary shortages.
- Link to identifying your state HAI coordinator:
<https://www.cdc.gov/hai/state-based/index.html>
- Link to healthcare coalition/preparedness:
<https://www.phe.gov/Preparedness/planning/hpp/Pages/find-hc-coalition.aspx>

-

Environmental Cleaning and Disinfection

- Routine cleaning and disinfection procedures are appropriate for COVID-19 in dialysis settings.
 - Ensure HCP have access to EPA-registered, hospital-grade disinfectants
 - Refer to the EPA-website for List N: Disinfectants for Use Against SARS-CoV-2: <https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2>
 - When using products from List N, facilities should ensure the products also have a bloodborne pathogen claim (e.g., hepatitis B, HIV).
- Any surface, supplies, or equipment located within 6 feet of symptomatic patients should be disinfected or discarded.

Patients Returning to Dialysis After Infection

What Did We Find?

- Patients took a lot longer to feel better than we expected.
- Many patients had symptoms for up to 4 weeks and some up six weeks.
- Once the patient felt better, had improved symptoms and met the CDC criteria, they were moved back to to dialyze in their regular dialysis spots.



CDC: Return to Outpatient Dialysis (July 2020)

- No Test-Based Strategy for Discontinuing Transmission-Based Precautions
- Symptom-Based Strategy for Discontinuing Transmission-Based Precautions.
- Patients with [mild to moderate illness](#) who are not severely immunocompromised:
 - At least **10 days** have passed *since symptoms first appeared* and
 - At least 24 hours have passed *since last* fever without the use of fever-reducing medications and
 - Symptoms (e.g., cough, shortness of breath) have improved
- Note: For patients who are **not severely immunocompromised¹** and who were **asymptomatic** throughout their infection, Transmission-Based Precautions may be discontinued when at least 10 days have passed since the date of their first positive viral diagnostic test.
- Patients with [severe to critical illness](#) or who are severely immunocompromised¹:
 - At least **20 days** have passed *since symptoms first appeared* and
 - At least 24 hours have passed *since last* fever without the use of fever-reducing medications and
 - Symptoms (e.g., cough, shortness of breath) have improved



SARS CoV-2 Vaccine

1. Is it safe for dialysis patients to receive this vaccine (and how do we know)?
2. Will dialysis patients mount a vigorous antibody response?
3. Will the vaccine protect dialysis patients with possibly suppressed immune systems as well as it protects others?
4. What should we be telling our patients about the facts we know and don't know?
5. What can we do to help both patients and staff feel comfortable with this vaccine?



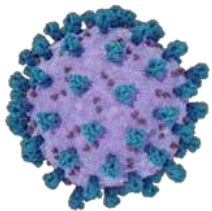
Long Haulers

- Patients have had systemic symptoms months after infection
- Neurologic
 - Fatigue, fuzzy head, short-term memory loss
 - Myalgia
 - Tremors
- Fevers; night sweats
- GI symptoms: nausea
- Bruising
- Arrhythmia
- Pain with deep breath



Summary

- Dialysis patients are at particular risk for COVID-19
- Home dialysis appears advantageous
- Dialysis patients may suffer neurologic, cardiac, GI, liver, clotting sequelae
- Long-haulers: How long? What can be done?
- Need clarity: What is the meaning of persistent + PCR in dialysis?
- Need data: Safety and Efficacy of SARS CoV-2 vaccines



ROLE OF NOVEL EXTRACORPOREAL THERAPIES

Saturday, March 6
16:25 – 16:50

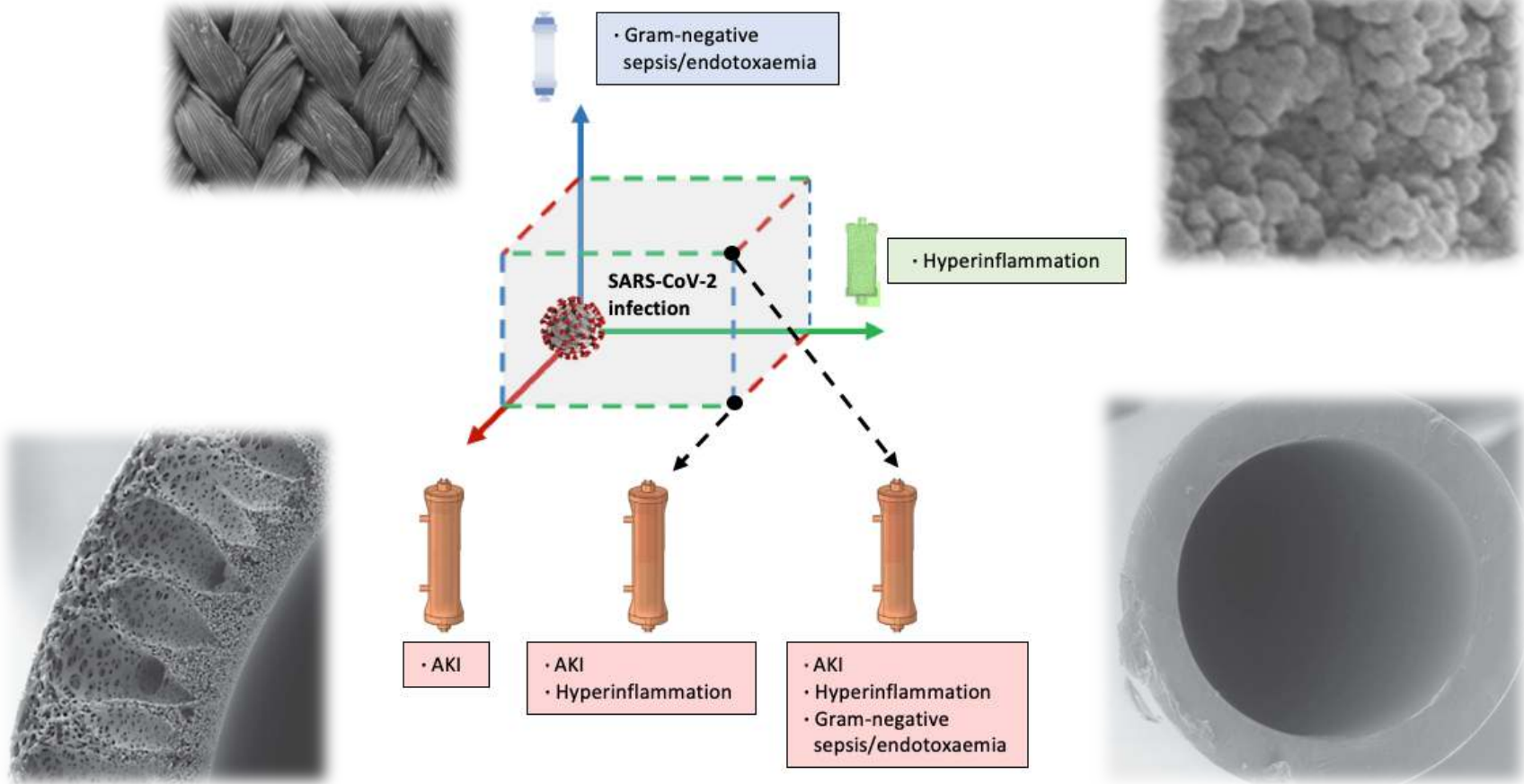
Thiago Reis, MD

- Research Affiliate at the International Renal Research Institute Vicenza - IRRIV - Vicenza, Italy.
- Head of Nephrology and Kidney Transplantation at Clínica de Doenças Renais de Brasília, Brazil.
- Department of AKI – Brazilian Society of Nephrology.
- PhD Candidate, Molecular Pharmacology Laboratory, University of Brasília – UnB.

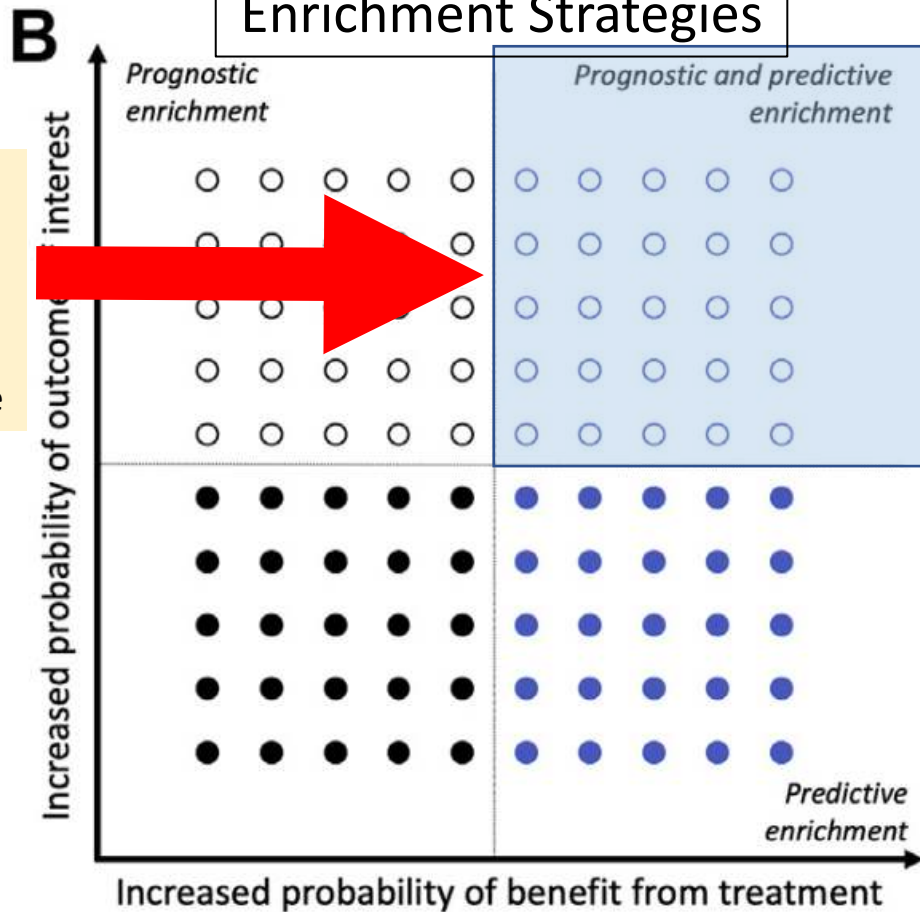
CONFLICT OF INTERESTS DISCLOSURE

In the last 3 years, TR has received funding for lectures, been consultant or part of advisory boards for Baxter, B.Braun, Contatti Medical (CytoSorb), Eurofarma and Jafron.

TRIDIMENSIONAL BLOOD PURIFICATION



Enrichment Strategies



Outcomes

NOT MORTALITY!!!

- PaO₂/FiO₂ increment
- Ventilator-free days
- Weaning of Noradrenaline

Patient Selection

BIOMARKERS

- [TIMP-2]•[IGFBP7]
- NGAL
- IL-6
- Endotoxin Activity

Severely ill
COVID-19 patient with
hyperinflammation



Research agenda

EBP INITIATION

Clinical Criteria

- Respiratory Index < 300
- New onset of LV dysfunction
- Acute kidney injury
- Fever
- Shock

Laboratory Criteria

- [TIMP-2]•[IGFBP7]
- NGAL
- Lymphocyte count
- Ferritin
- Lactate dehydrogenase
- D-dimer
- C-reactive protein
- Myoglobin
- Troponin
- IL6
- Procalcitonin
- Endotoxin activity*
- Endotoxin concentration*
- Culture-proven Gram-negative sepsis*



- Validate clinical and laboratory plausible criteria for EBP initiation, monitoring and discontinuation.
- Apply in the context of RCT

EBP MONITORING

Clinical Criteria

- Respiratory Index
- LV ejection fraction
- Kidney function
- Fever
- Shock

Laboratory Criteria

- [TIMP-2]•[IGFBP7]
- NGAL
- Lymphocyte count
- Ferritin
- Lactate dehydrogenase
- D-dimer
- C-reactive protein
- Myoglobin
- Troponin
- IL6
- Procalcitonin
- Endotoxin activity*
- Endotoxin concentration*
- Culture-proven Gram-negative sepsis*



EBP DISCONTINUATION

Consider following
manufacture's instructions.

Usually for cytokine removal:

3 consecutive days
2 to 12 hours

Usually for endotoxin removal:

2 consecutive days
2 to 4 hours

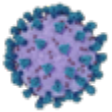
Evaluate re-prescription
accordingly to patient's
evolution



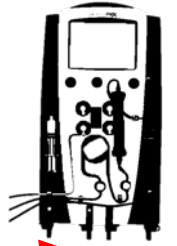
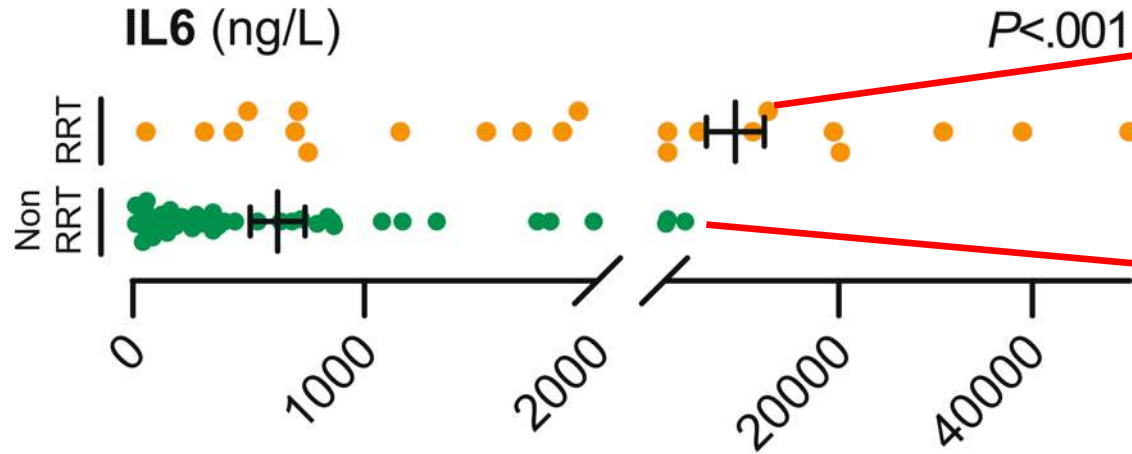
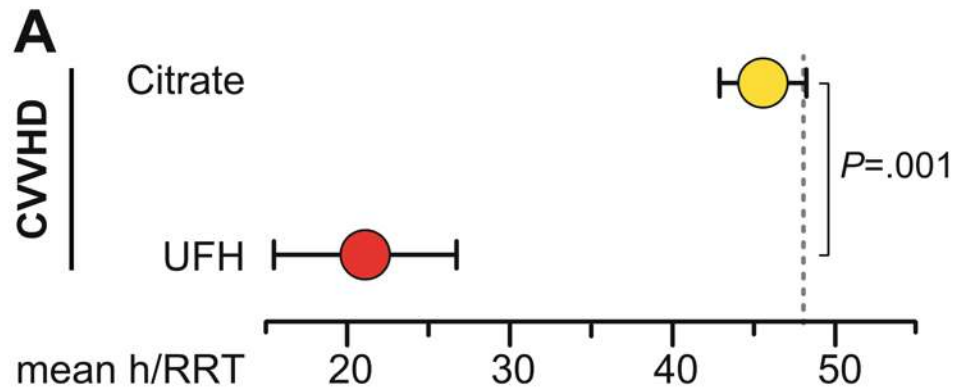
Retrospective



Single-center



n=71



A

CWHD

Citrate

UFH

CRRT PATIENTS DO HAVE
HIGH IL-6!!!

Retrospective

0

1000

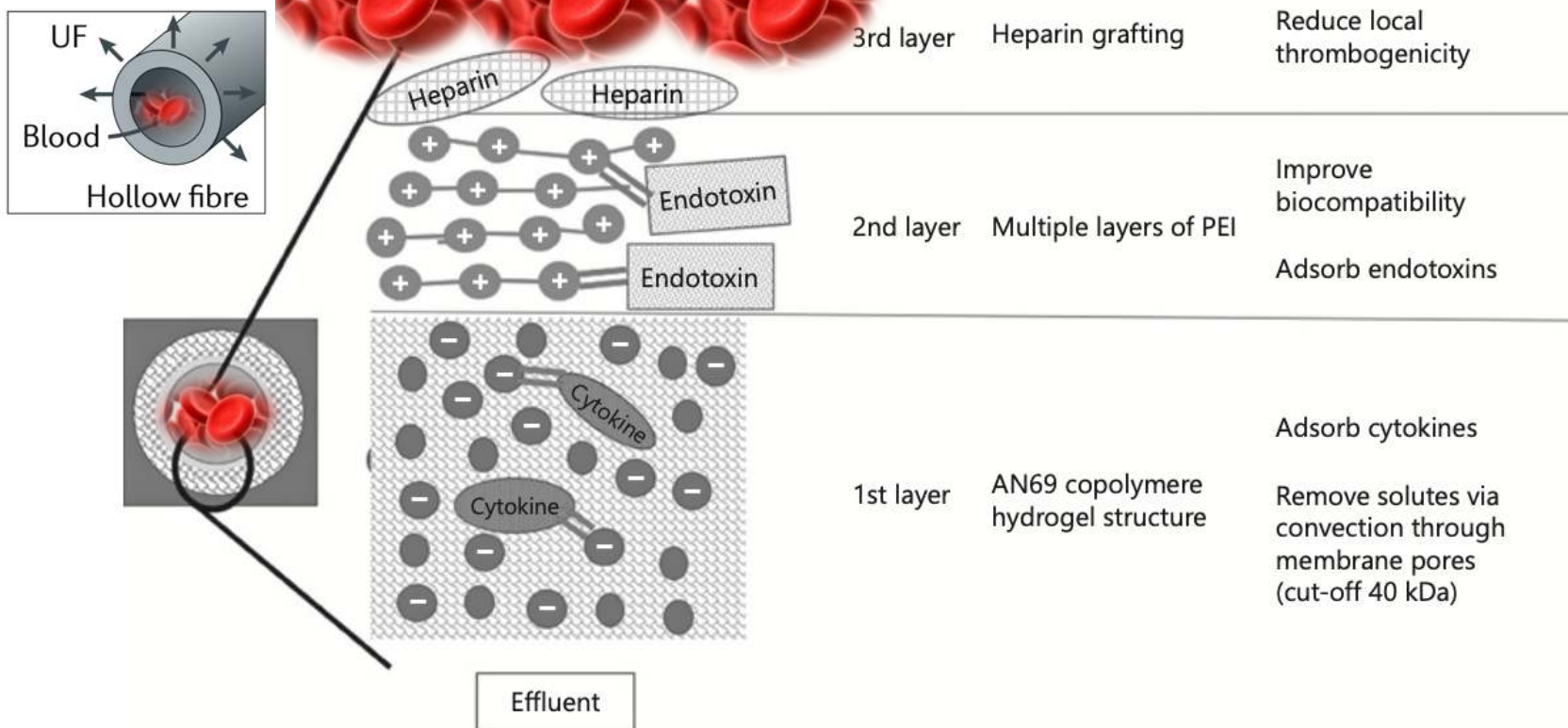
2000

20000

40000



ACRYLONITRILE – AN69



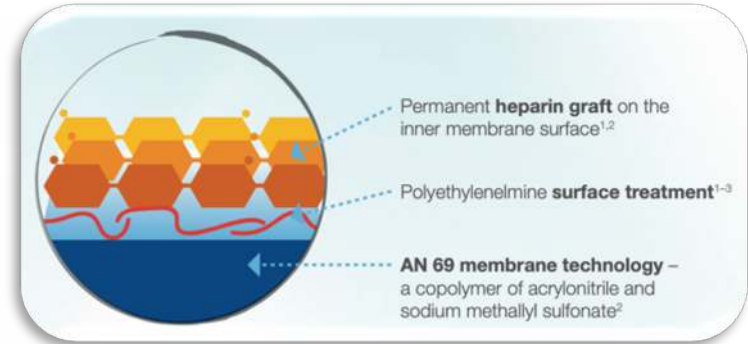
ACRYLONITRILE – AN69



Heparin

**High density polyethylenimine
(30 mg/m²)**

Polyacrylonitrile



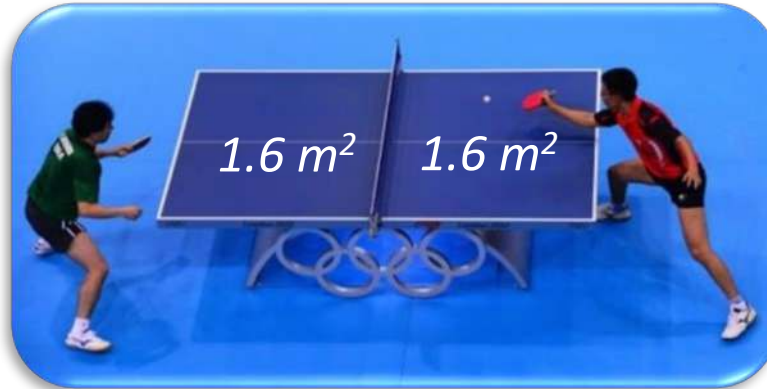
→ **Endotoxins**

→ **Cytokines**

HYDROGEL - 17,000 m²



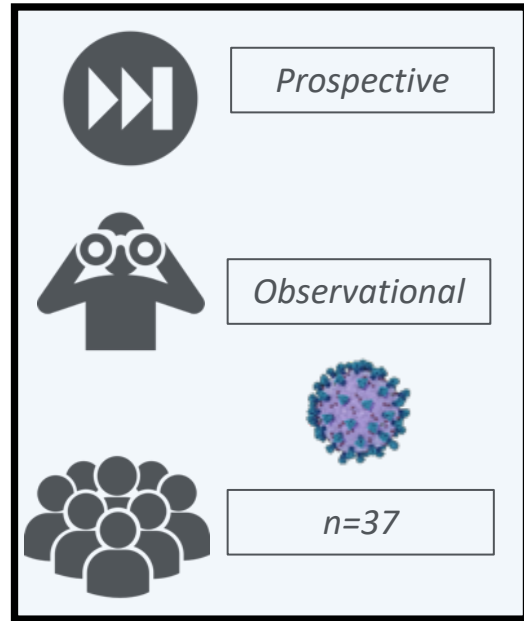
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BLOOD PURIFICATION COVID-19



INDICATION TO START

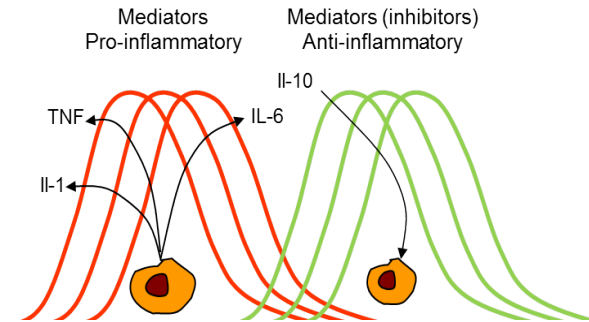
AKI \rightarrow 70%

- AKI Stage 2 \rightarrow 23%
- AKI Stage 3 \rightarrow 77%

Immunomodulation \rightarrow 30%

AKI Stage 1

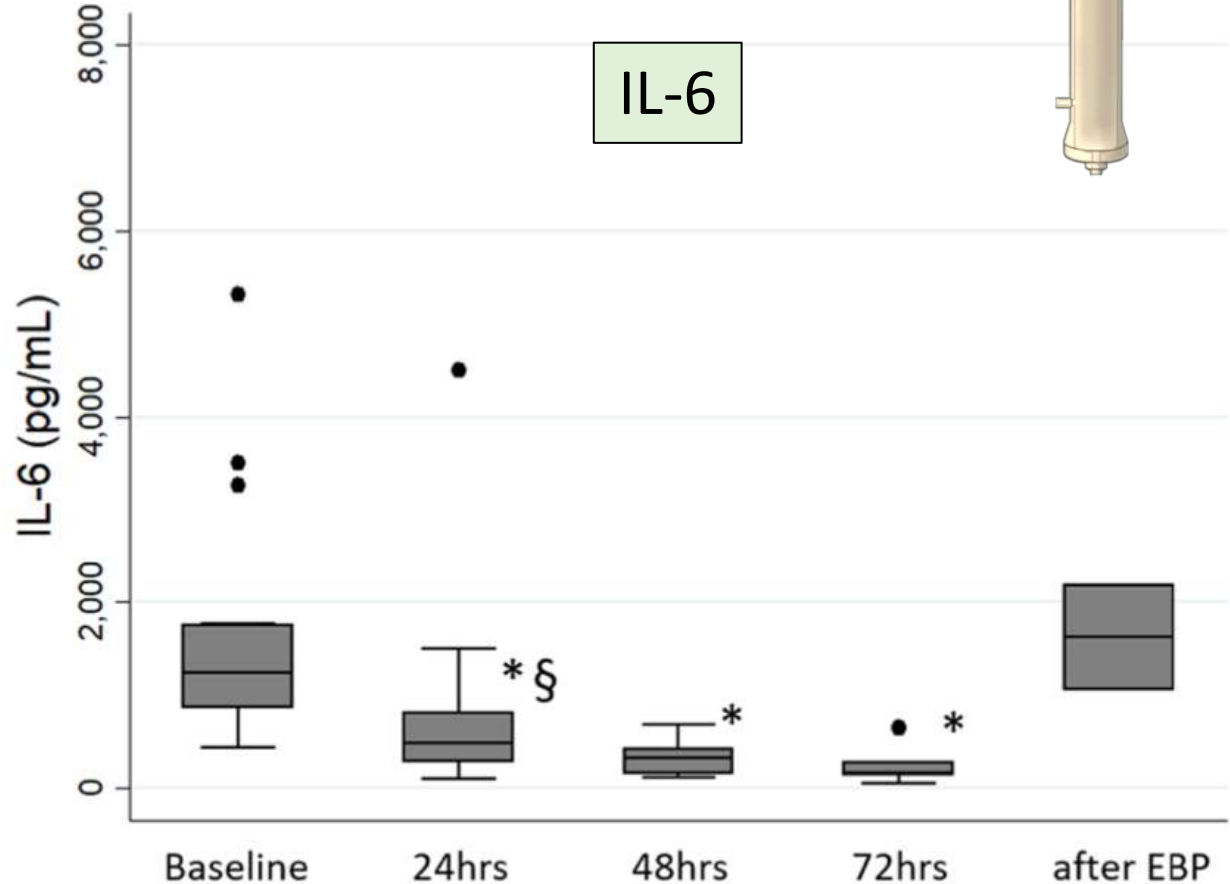
- Fluid overload \rightarrow 40%
- Uremic control \rightarrow 49%
- Electrolytes \rightarrow 24%



BLOOD PURIFICATION COVID-19

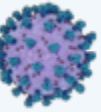


IL-6



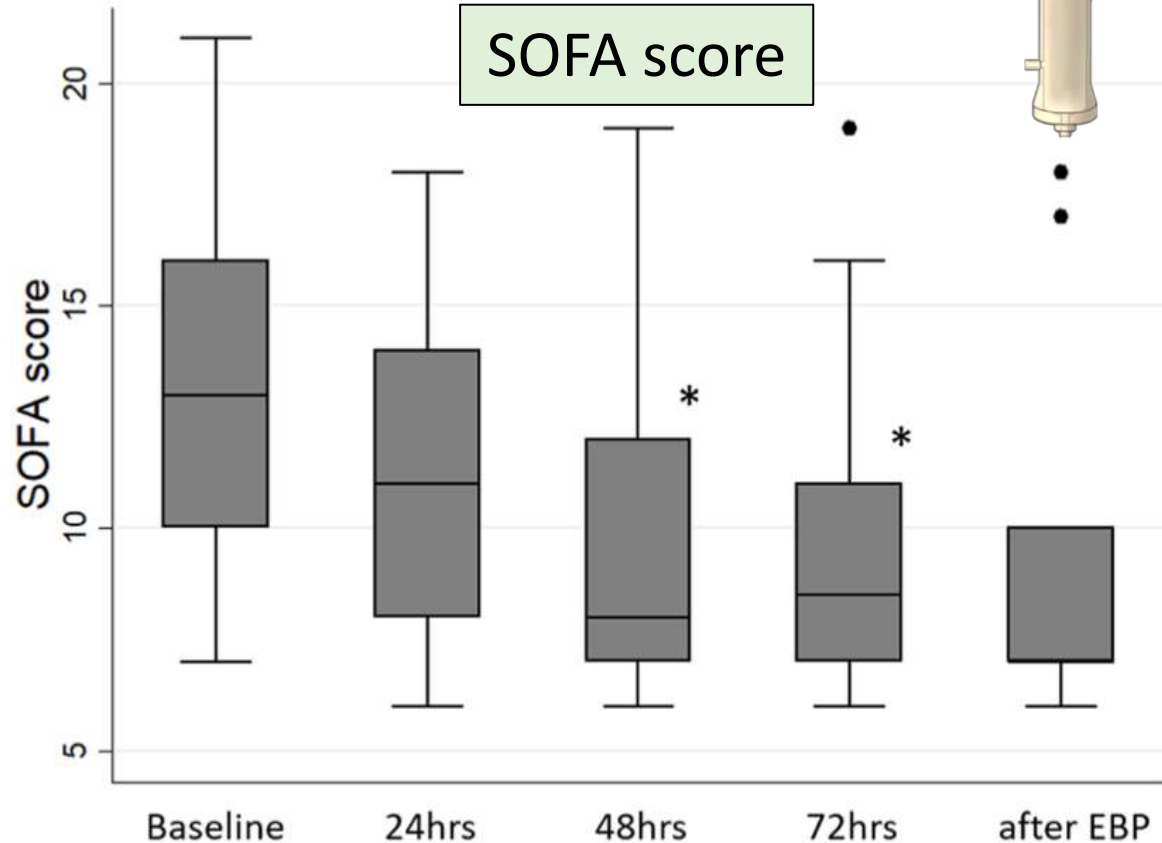
Prospective

Observational



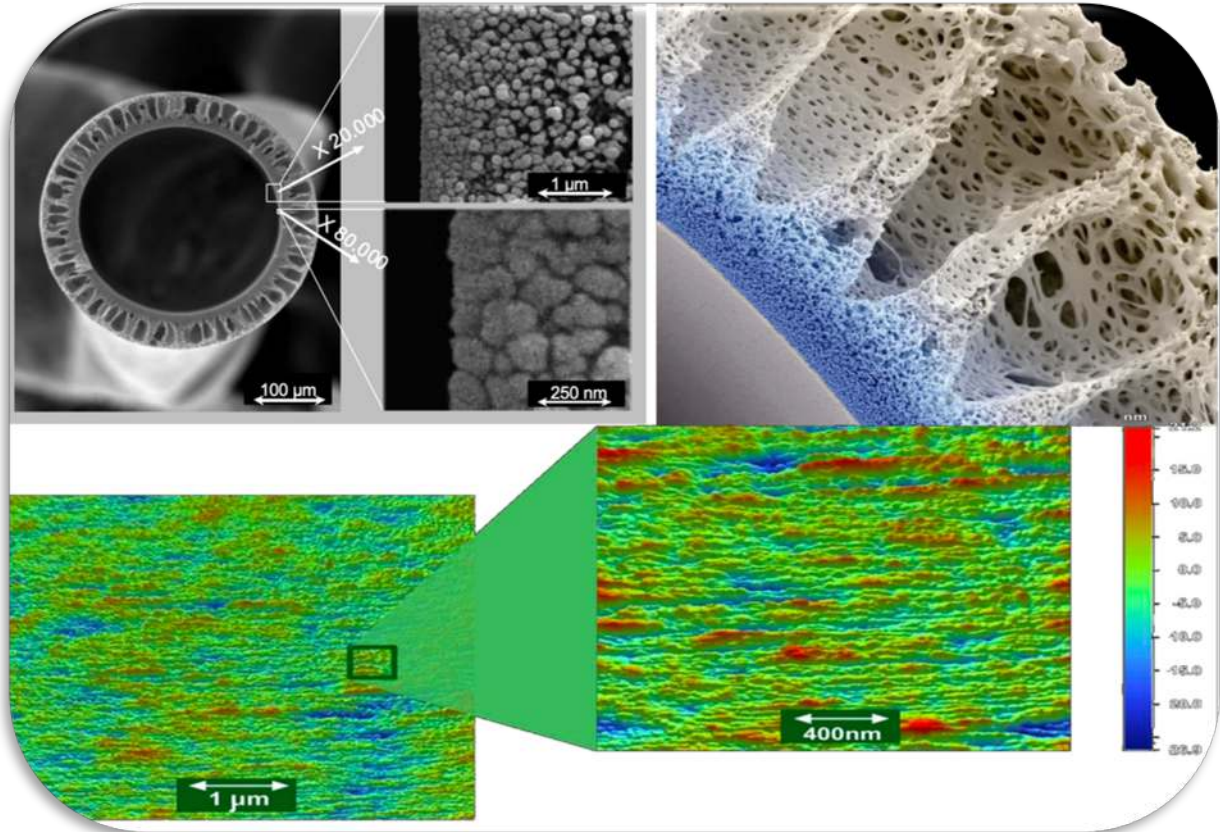
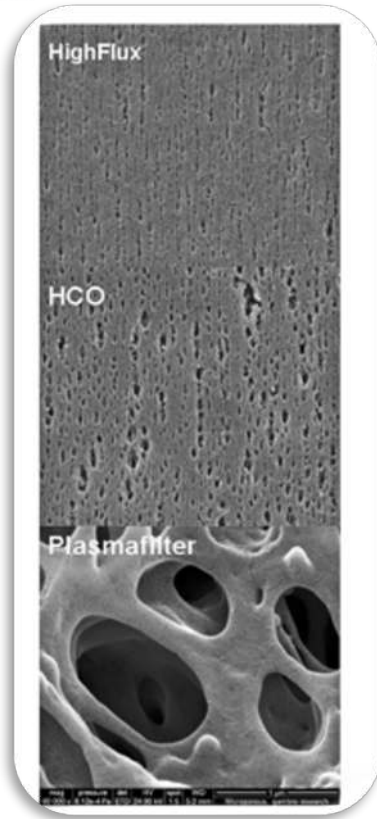
n=37

BLOOD PURIFICATION COVID-19



Villa G, Romagnoli S, De Rosa S, et al. Blood purification therapy with a hemodiafilter featuring enhanced adsorptive properties for cytokine removal in patients presenting COVID-19: a pilot study. Crit Care. 2020;24:605. Published 2020 Oct 12.

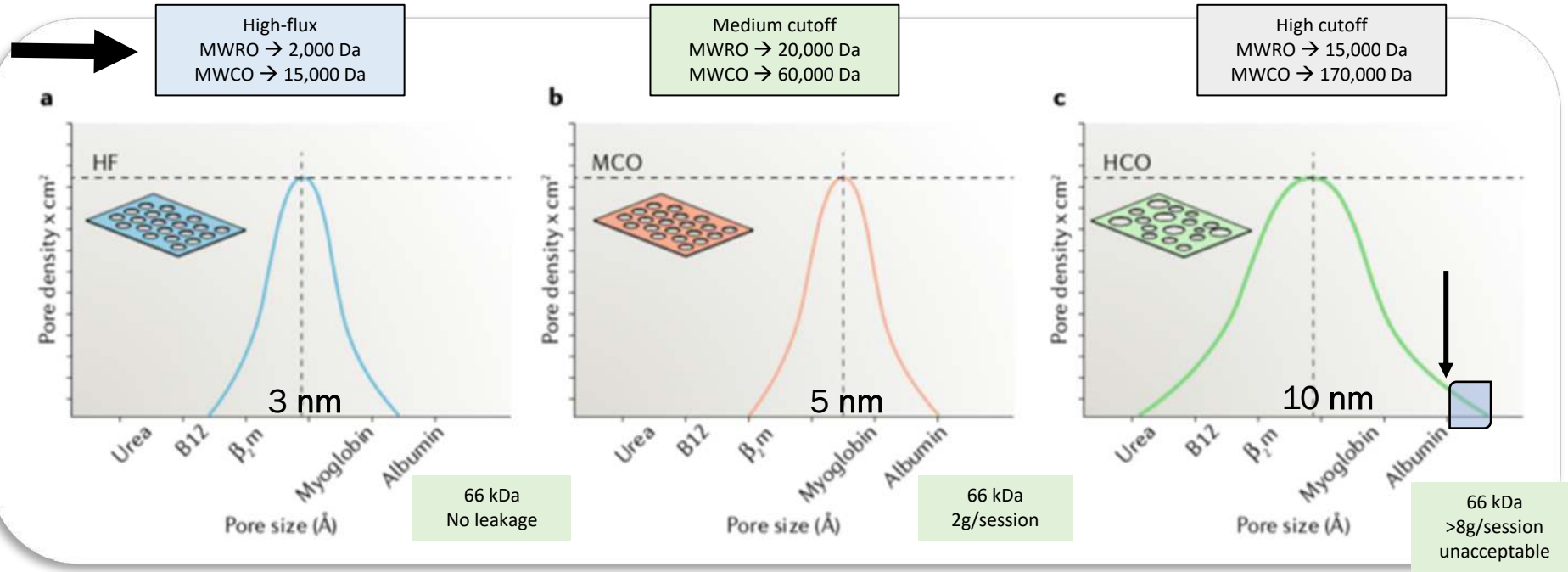
POLYETHERSULFONE



-Ronco C, Clark WR. Haemodialysis membranes. Nat Rev Nephrol. 2018;14(6):394-410.

Boschetti-de-Fierro et al. Extended characterization of a new class of membranes for blood purification: the high cut-off membranes. Int J Artif Organs. 2013 Jul;36(7):455-63.

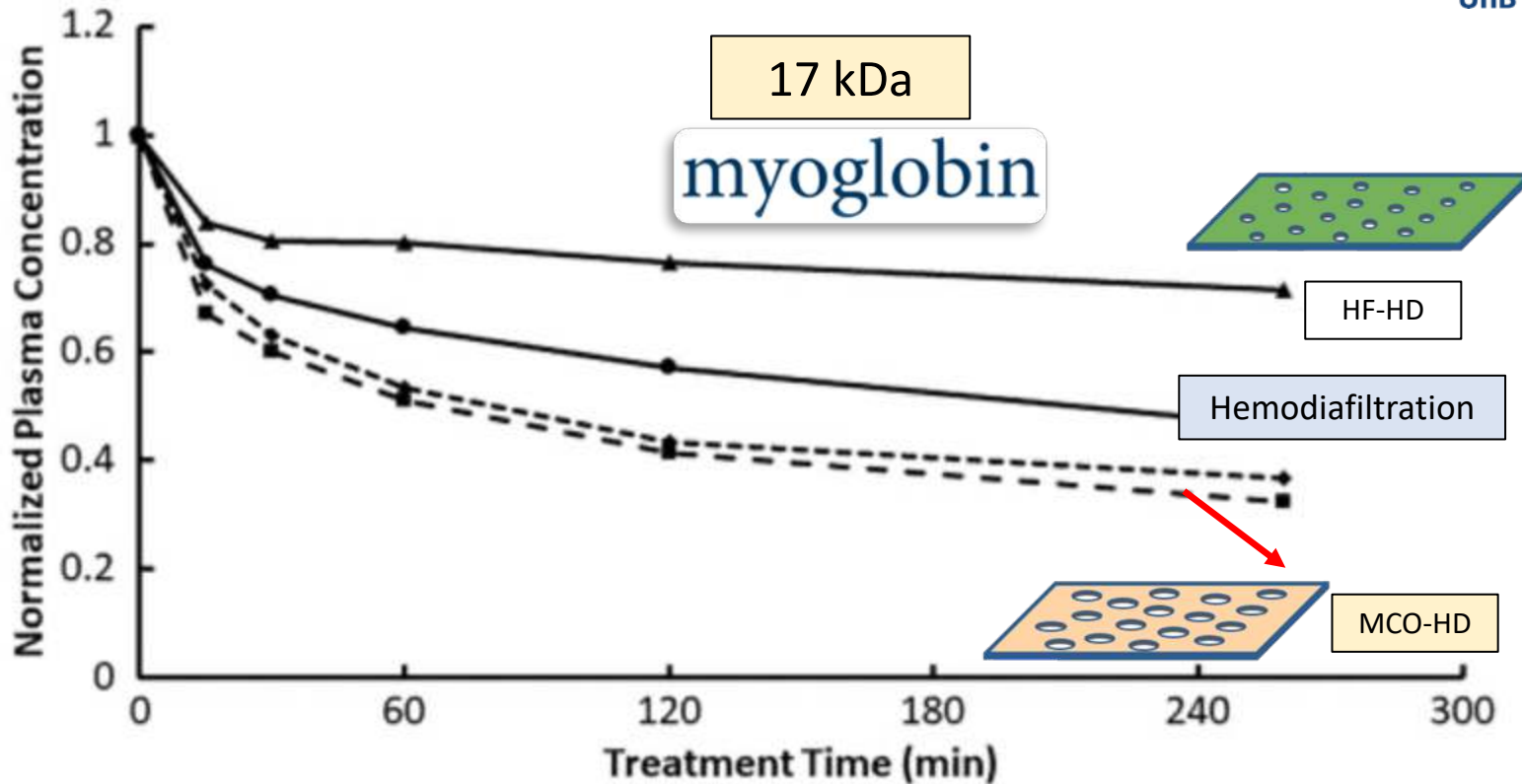
ALBUMIN LEAKAGE

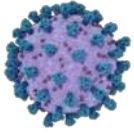


-Ronco C, Clark WR. Haemodialysis membranes. Nat Rev Nephrol. 2018;14(6):394-410.

Boschetti-de-Fierro et al. Extended characterization of a new class of membranes for blood purification: the high cut-off membranes. Int J Artif Organs. 2013 Jul;36(7):455-63.

MEDIUM CUTOFF vs HIGH-FLUX





WORLD HEALTH ORGANIZATION DECLARES

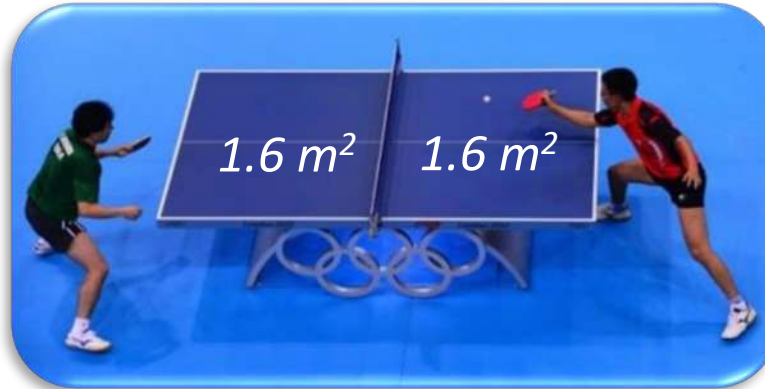
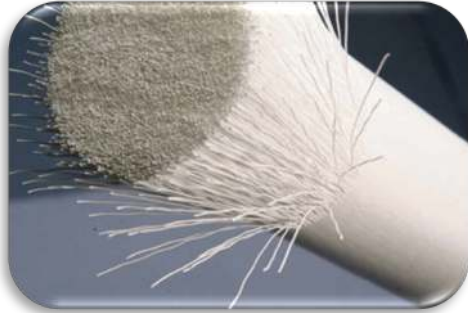


REMOVE CYTOKINES!!!

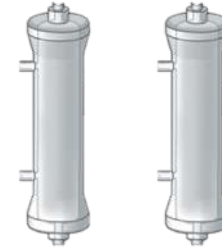
HEMOPERFUSION – 60,000 m²



=



=



HEMOPERFUSION + ECMO



CYCOV-II

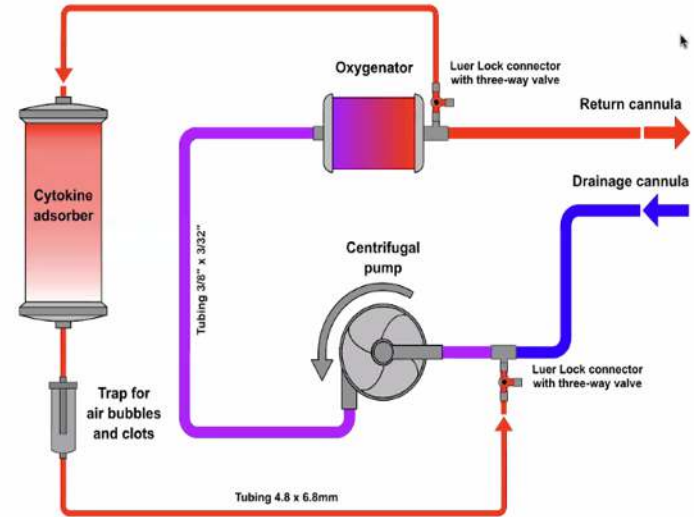
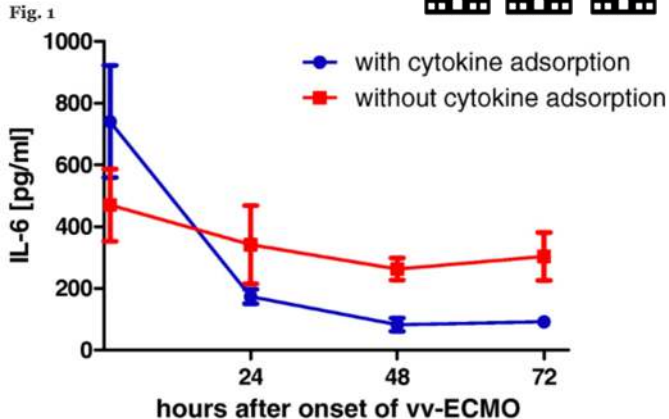
-Randomized



-Open-label

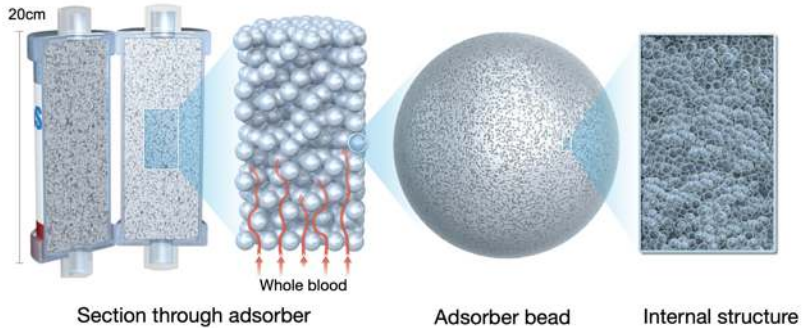
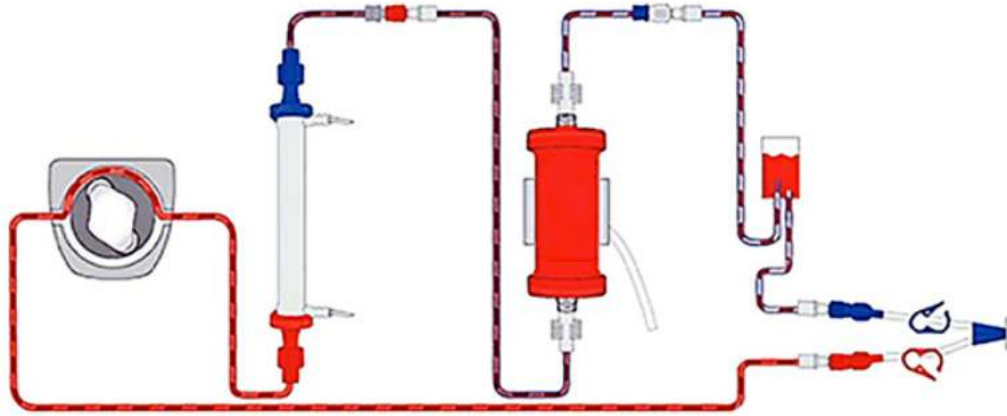


-Multicentric



- 1.Rieder M et al. Cytokine Adsorption in Severe Acute Respiratory Failure Requiring Veno-Venous Extracorporeal Membrane Oxygenation. ASAIO J. 2020 Nov 9.
- 2.Rieder M et al. Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation. Crit Care. 2020;24(1):435. Published 2020 Jul 14.

HEMOPERFUSION + CRRT



1. Al Shareef K, Bakouri M. Cytokine Blood Filtration Responses in COVID-19 [published online ahead of print, 2020 May 28]. *Blood Purif.* 2020;1-9.
2. Reis T, unpublished data.

HEMOPERFUSION + CRRT



Not COVID-19



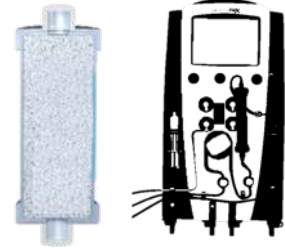
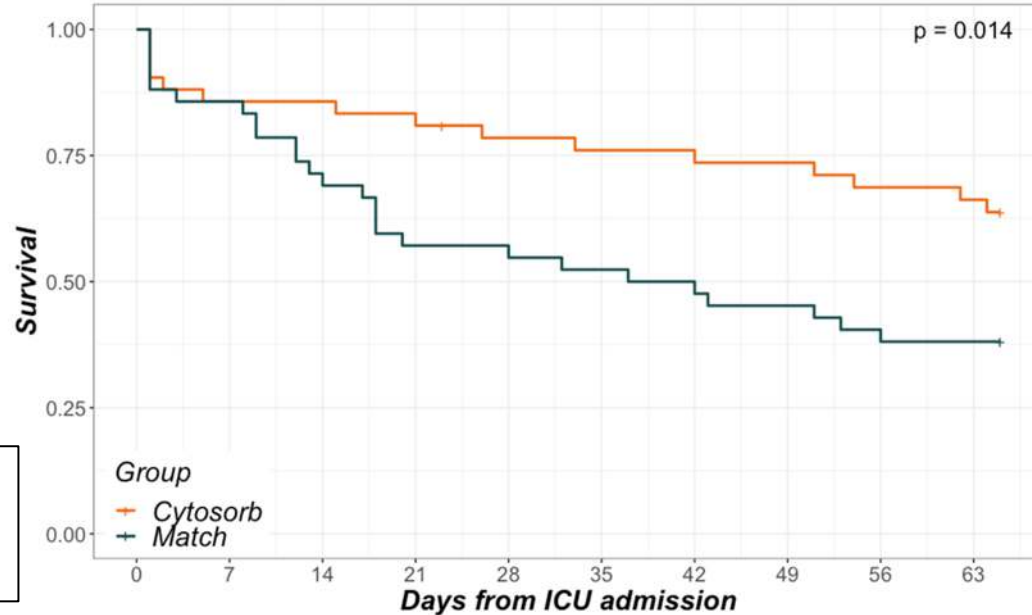
Retrospective



Single-center



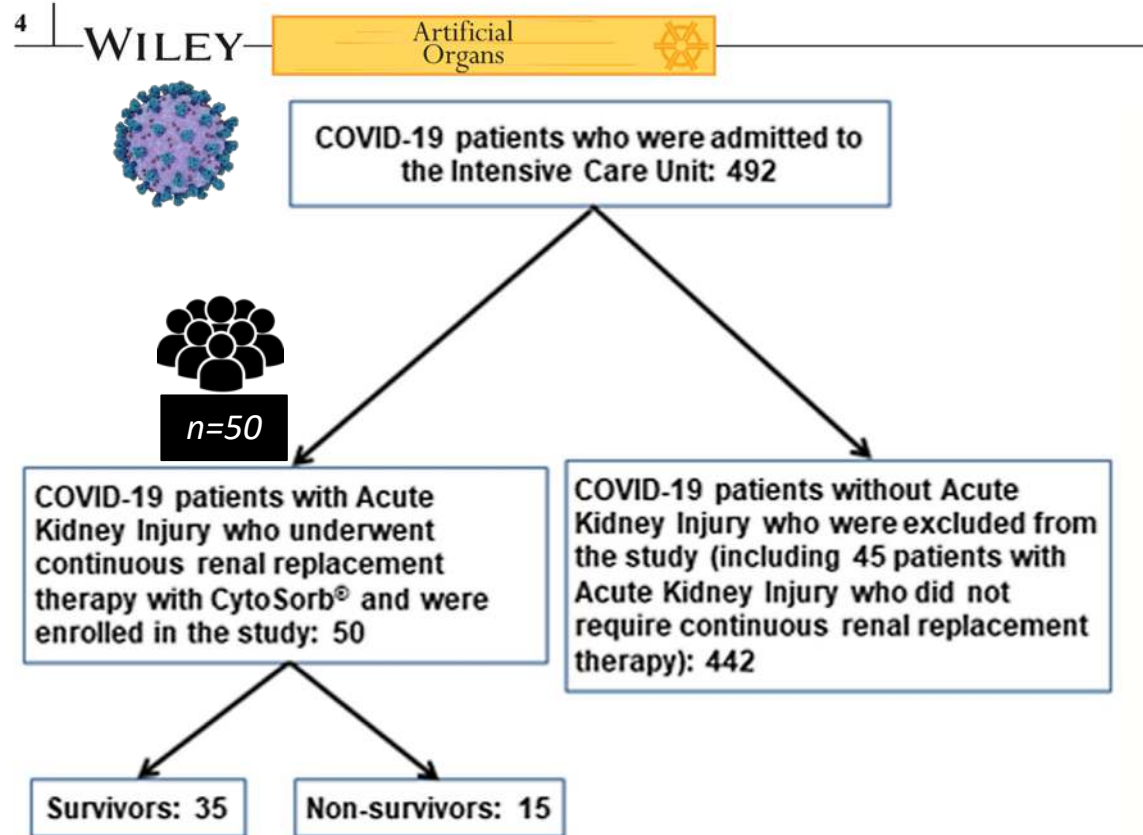
CASE n=42
vs
CONTROL n=42



VS



HEMOPERFUSION + CRRT



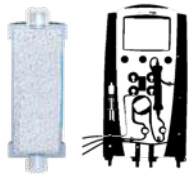
Case series



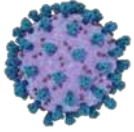
Retrospective



Single-center



CRRT
+
Hemoperfusion

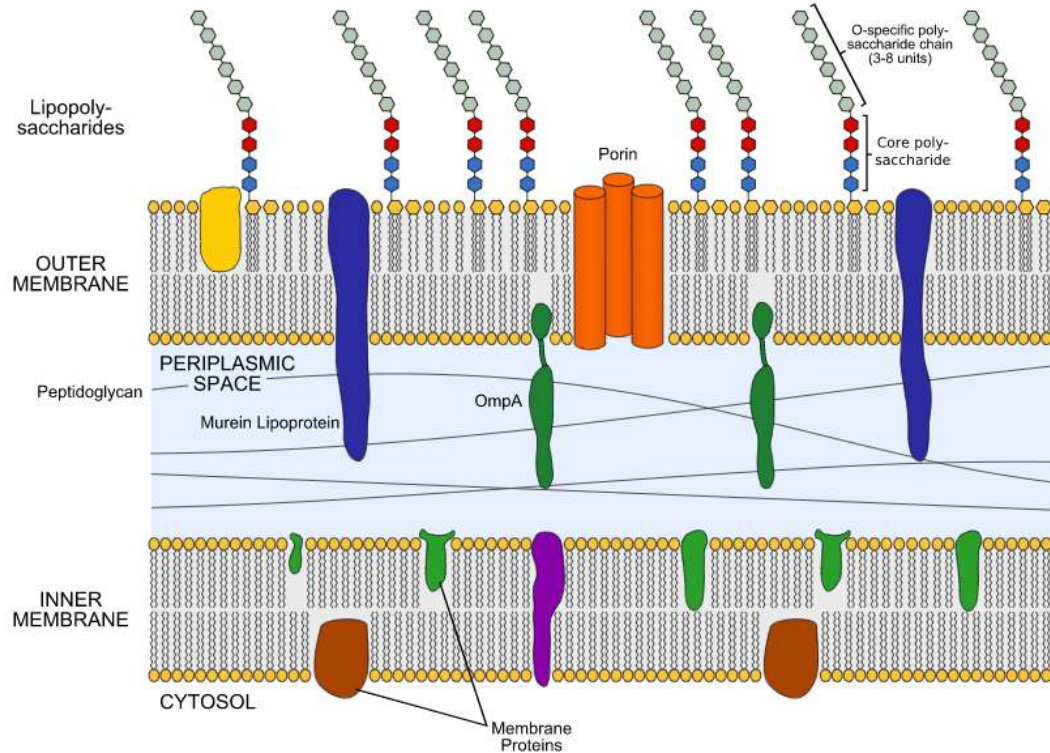


GRETA ALSO DECLARED

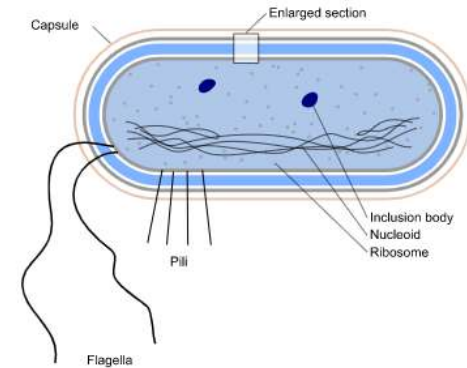


ENDOTOXINS

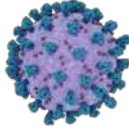
LIPOPOLYSACCHARIDES



Gram Negative Bacterial Cell Wall



ENDOTOXEMIA



Hospitalized with COVID-19

147

Source Population

No evidence of pneumonia

COVID-19 Pneumonia

53

No leftover samples

Fulfilled inclusion criteria

19

Final Cohort

EAA >0.6

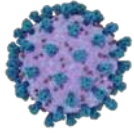
High EAA at day 1

8

Low EAA at day 1

11

PMX-HEMOPERFUSION



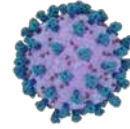
Case series

Retrospective

Multicenter

*PMX
Hemoperfusion*

n=12



Case series

Retrospective

Single-center

*PMX
Hemoperfusion*

n=12

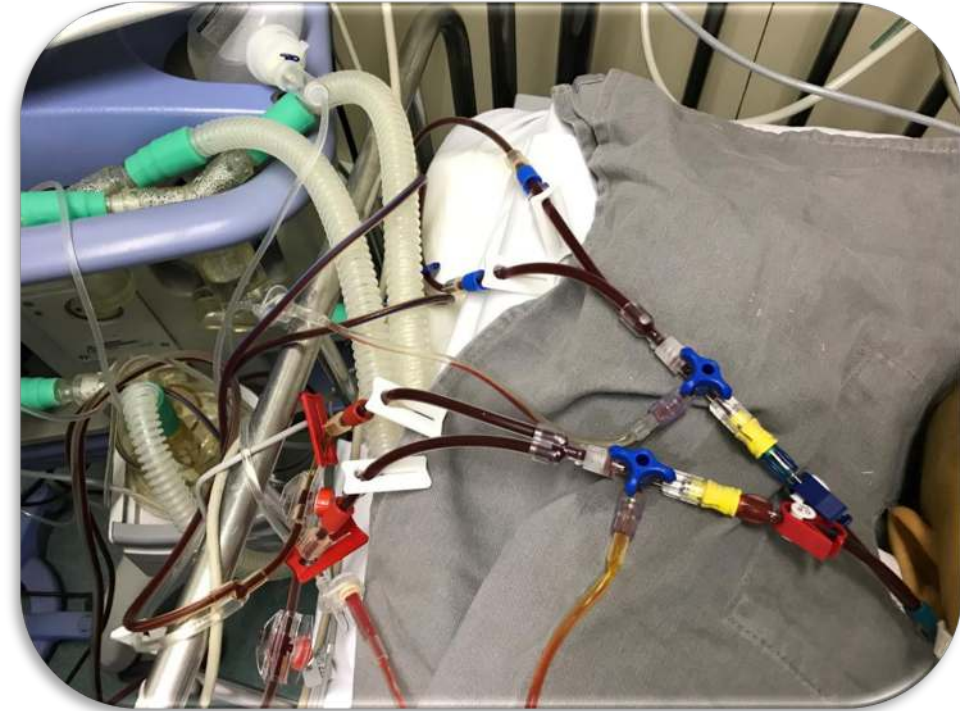
1. De Rosa S, Cutuli SL, Ferrer R, Antonelli M, Ronco C; COVID19 EUPHAS2 Collaborative Group. Polymyxin B hemoperfusion in COVID-19 Patients with endotoxic shock: Case Series from EUPHAS II registry [published online ahead of print, 2020 Dec 30]. *Artif Organs*. 2020
2. Katagiri D et al. Direct hemoperfusion using a polymyxin B-immobilized polystyrene column for COVID-19 [published ahead of print, 2020 Dec 15]. *J Clin Apher*. 2020

FAUCI DECLARED



GET RID OF ENDOTOXINS!!!

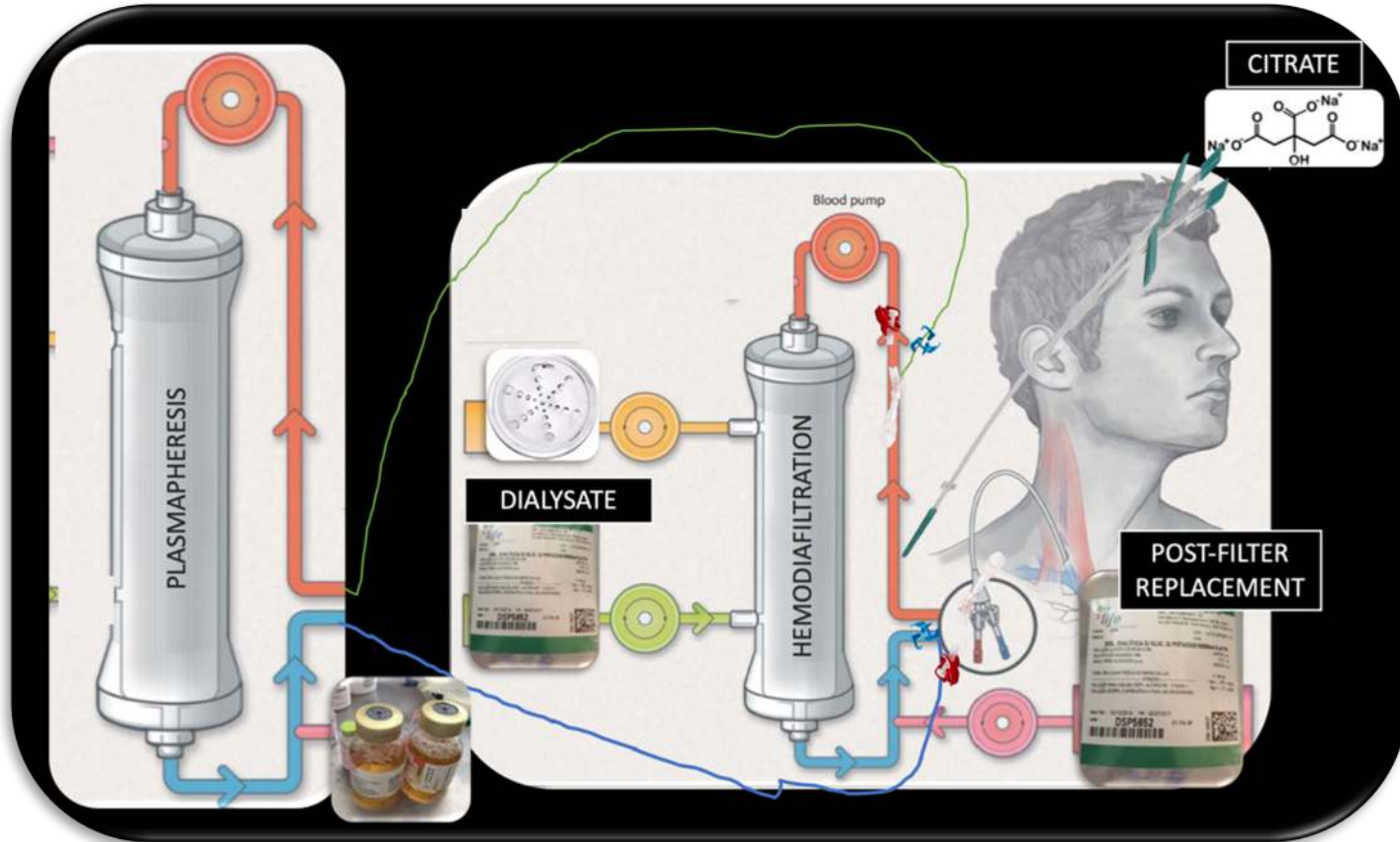
PLASMAPHERESIS + CRRT



1. Gucyetmez B, Atalan HK, Sertdemir I, Cakir U, Telci L; COVID-19 Study Group. Therapeutic plasma exchange in patients with COVID-19 pneumonia in intensive care unit: a retrospective study. Crit Care. 2020;24(1):492. Published 2020 Aug 8.

2. Watanabe A, unpublished data.

PLASMAPHERESIS + CRRT



1. Gucyetmez B, Atalan HK, Sertdemir I, Cakir U, Telci L; COVID-19 Study Group. Therapeutic plasma exchange in patients with COVID-19 pneumonia in intensive care unit: a retrospective study. Crit Care. 2020;24(1):492. Published 2020 Aug 8.

2. Reis T, unpublished data.

PLASMAPHERESIS



Retrospective



D-dimer
Cutoff 2 mg/L



n = 73



Higher mortality in
TPE negative group

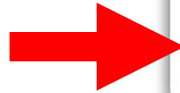


Table 2 Comparisons of laboratory parameters in pre and post-TPE procedure

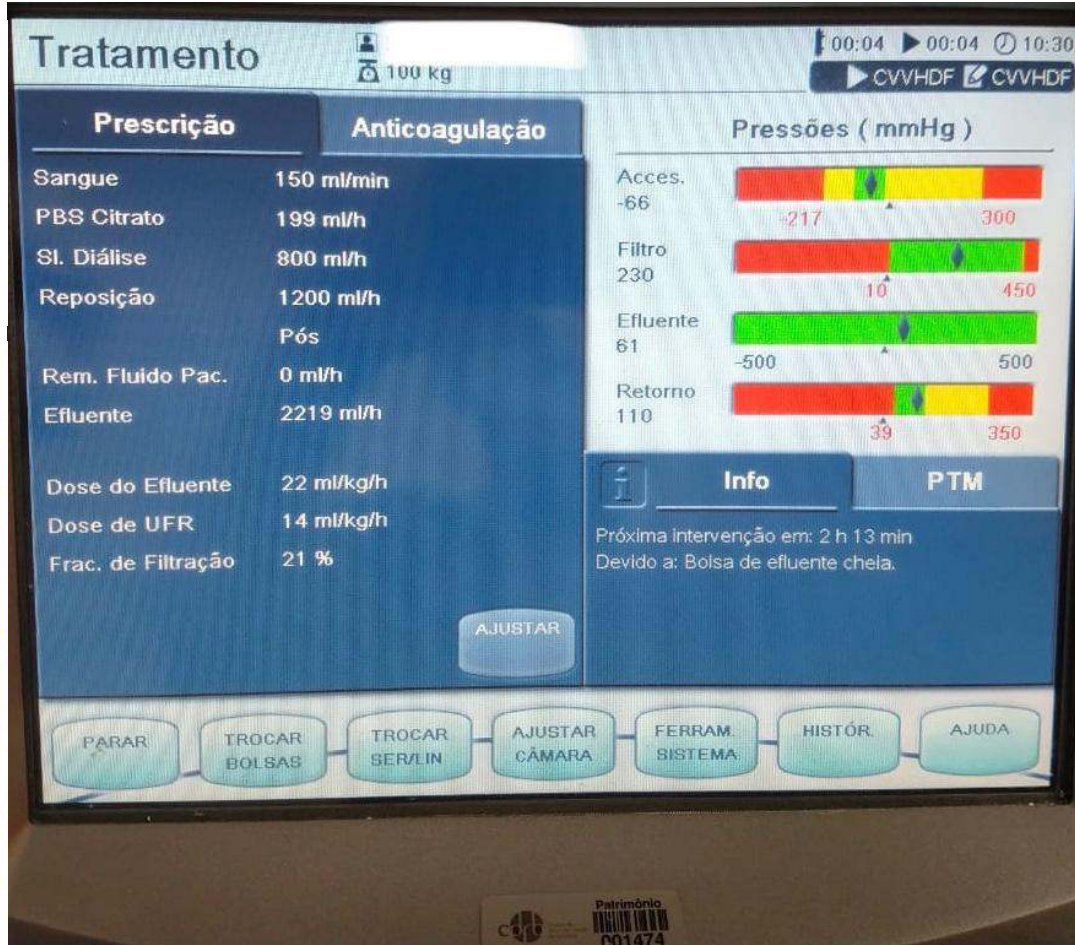
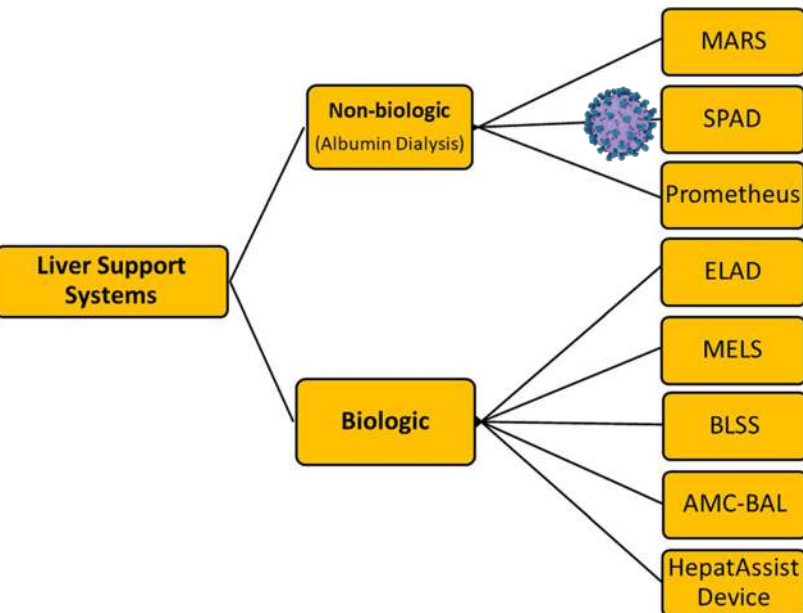
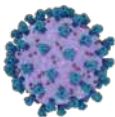
	Pre-TPE	Post-TPE	<i>p</i>
WBC ($\times 10^3/\mu\text{L}$)	9.08 \pm 4.1	9.14 \pm 3.5	0.951
Neuc ($\times 10^3/\mu\text{L}$)	7.38 \pm 3.1	7.33 \pm 3.3	0.953
Lymc ($\times 10^3/\mu\text{L}$)	0.9 (0.5–1.3)	1.02 (0.77–1.27)	0.053
NLCR	6.8 (1.8–11.7)	6.7 (4.2–9.2)	0.184
LDH (IU/L)	436 (322–550)	239 (181–297)	0.001
D-dimer (mg/L) ^{&}	7.8 (2.1–35.2)	1.3 (0.6–3.9)	< 0.001
Ferritin (ng/mL) ^{&}	1268 (399–6110)	405 (157–1650)	0.001
IL-6 (pg/mL) ^{(13)&}	161 (36.2–2958)	24.5 (1.5–130)	0.001
CRP (mg/dL) ^{&}	11.8 (0.4–29.7)	0.9 (0.3–7.2)	< 0.001
Procalcitonin (ng/mL) ^{&}	0.27 (0.02–87)	0.1 (0.01–39)	0.002

REVIEW

Open Access

Bile cast nephropathy: when the kidneys turn yellow

Alissar El Chediak^{1†}, Khaled Janom^{2†} and Sahar H. Koubar^{3*}



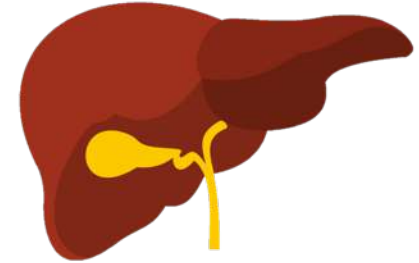
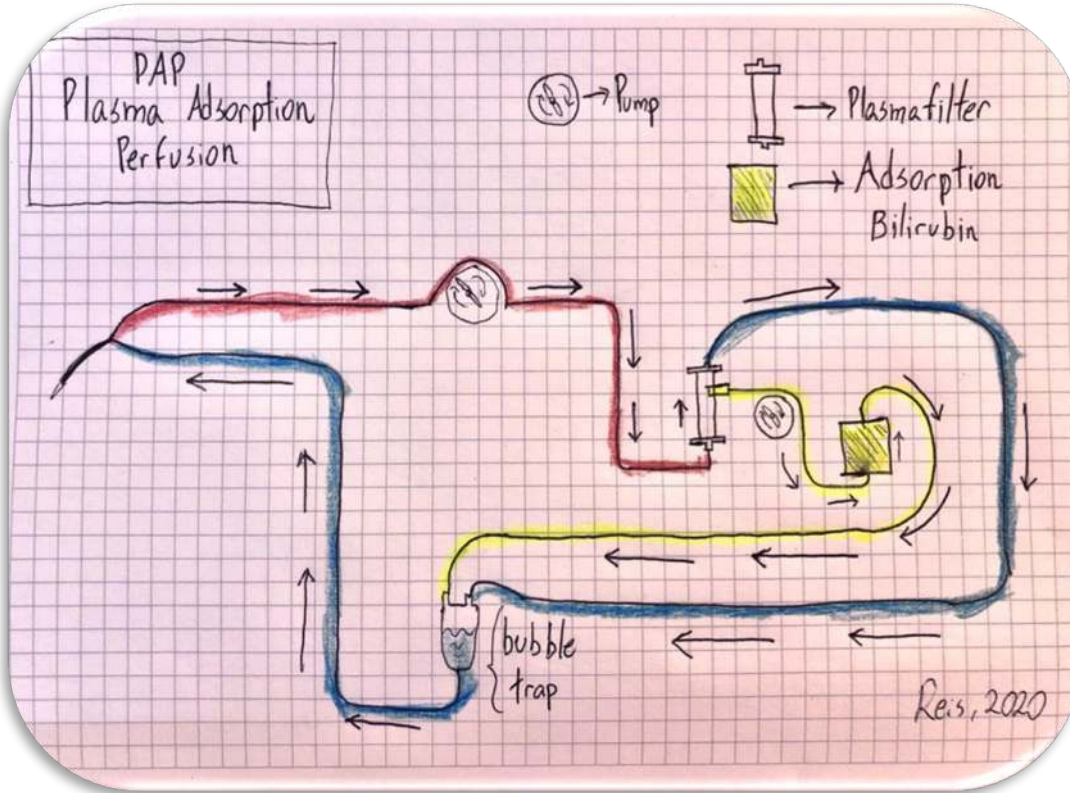
SINGLE-PASS ALBUMIN DIALYSIS



-Schmuck RB et al. Single Pass Albumin Dialysis-A Dose-Finding Study to Define Optimal Albumin Concentration and Dialysate Flow. *Artif Organs*. 2017 Feb;41(2):153-161

-Sponholz C et al. Molecular adsorbent recirculating system and single-pass albumin dialysis in liver failure--a prospective, randomised crossover study. *Crit Care*. 2016;20:2. Published 2016 Jan 4.

PLASMA ADSORPTION PERFUSION

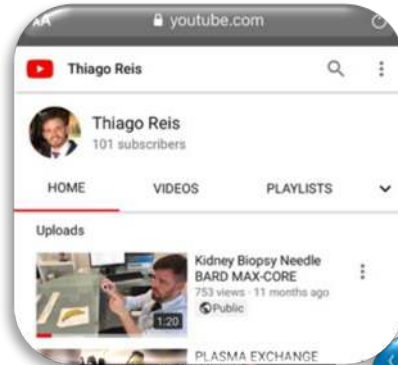


1. Viggiano D, de Pascale E, Marinelli G, Pluvio C. A comparison among three different apheretic techniques for treatment of hyperbilirubinemia. J Artif Organs. 2018 Mar;21(1):110-116.
2. Donati G. Detoxification of bilirubin and bile acids with intermittent coupled plasmafiltration and adsorption in liver failure (HERCOLE study). J Nephrol. 2020 Jul 24.



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