

FAQ for hemoperfusion application and operation in COVID-19 pandemic fighting

1. How does HA330/HA380 hemoperfusion therapy benefit the COVID-19 patients?

HA330 is clinically specifically used for critical illness such as sepsis, septic shock and others at the early or middle stage of a cytokine storm onset. Based on adsorption technology with the adsorbent called neutral macro-porous resin, the porosity structure of the adsorbing beads allows HA330 to absorb excessive cytokines. Thus, during the COVID-19 pandemic, the HA330 plays an important role in cytokine removal, hemodynamic stabilizing and immune function regulation for severe and critically ill patients with/without COVID-19 infection.

2. How to recognize the Cytokine storm in COVID-19?

In some COVID-19 patients, the IL-6 level is far lower than that in sepsis patients. Perhaps because the cytokine storm does not occur among all COVID-19 patients and we should pay more attention to patients with higher IL-6 levels, or choose other biomarkers such as ferritin, D-dimer, and even relevant clinical signs such as O₂ situation to evaluate the onset of cytokine storms. With the timely identification and the intervention of extracorporeal therapy, it would help to prevent the sudden crash of patients undergoing cytokine storm clinically.

3. When and how to choose the COVID-19 patients for hemoperfusion?

There is no doubt that the earlier intervention with hemoperfusion, the more benefits for the COVID-19 patients.

To choose the right COVID-19 patients as early as possible according up to dates evidences and clinical experience, there are two aspects needed comprehensive consideration. One is clinical symptoms, signs or diagnosis such as increased dyspnea, uropenia, unconsciousness, increased limb edema; hemodynamic instability needed vasopressors, respiratory failure or extra-pulmonary organ failure, shock, etc. Another is medical evidences such as CT scan progress with pulmonary lesions > 50% within 24-48 hours, abnormal biomarkers with such as elevated inflammatory mediators and indexes, abnormal coagulation index, etc. Here below are some criteria for your references.

1) *From Prof. Claudio Ronco,*

(Director of the Department of Nephrology International Renal Research Institute, Sr Bortolo Hospital, Vicenza, Italy)

- *Patients without AKI or at stage I AKI*
- *High SOFA score*
- *Mechanical ventilation*
- *Hemodynamic instability and need of vasopressors*
- *High AKI bio markers*
- *Status of inflammation (CRP, IL-6, PCT, Ferritin)*

2) *From Dr. Omender Singh*

(Director of the Institute of Critical Care Medicine, Max Health Care, India)

- *Patients with Moderate, Severe, and Critical/Life Threateningly ill COVID-19 should be screened for hyper-inflammation using laboratory trends to identify the subgroup of patients for whom Extracorporeal Cytokine Adsorption could improve mortality.*
- *Ferritin >500ng/mL;*
- *C-Reactive Protein (CRP) >70mg/L;*
- *D-Dimer >1000ng/mL;*
- *Lactate Dehydrogenase (LDH) >300U/L;*
- *Lymphocyte Count <0.8 billion/L)*

3) *From Prof. Ricard Ferrer*

(Head of Intensive Care Department, Vall d'Hebron University Hospital, Barcelona, Spain)

- *Covid-19 pneumonia and Hyper inflammatory State Indications of Hemoperfusion*
- *IL-6 >1000 pg/mL,*
- *D-dimer > 1500 ng/ml*
- *Ferritin > 500 ng/ml.*
- *ARDS not responding to prone position (PaO₂/FiO₂ ratio > 100 mmHg)*

4. *What kinds of COVID-19 patients are not recommended for hemoperfusion?*

Generally speaking, there are several considerations that we don't recommend hemoperfusion for patients when they have been under long-term use of immunosuppressant or with immune deficiency, have severe anemia (hemoglobin \leq 60g/L) without correct, have malignant tumor, have very low chance to survive.

5. *What's the duration of HA330/HA380 hemoperfusion for COVID-19 patients?*

It was recommended to maintain the HA330/HA380 for COVID-19 patients for 2-6 hours, and in some cases it can be up to 12 hours.

6. *How much HA330/HA380 cartridges the COVID-19 patients need?*

In one newest publication for COVID-19, Prof. Claudio Ronco points out the 2-1-1 therapy recommendation for the severe COVID-19 patients; this is 2 times of hemoperfusion treatment per first 24 hours, followed by once each day for two days.

7. What's the different between HA330 & HA380 during COVID-19?

During the COVID-19 in China, both HA330 and HA380 play important role. Since HA380 is an optimized model based on HA330, with less blood volume in the cartridge, which means, while removing the cytokine such as HA330, the patient's extracorporeal blood volume will be less than HA330, which may benefit the hemodynamic in some degree. The capability of removing cytokine of HA380 is higher than HA330, which means according to the Guideline, Experts consensus, clinical doctors can do adjustment based on the suggested "2-1-1 therapy" recommendation, such as prolonging therapy days after the third day or increasing the treatment frequency from the second day...etc., all this adjustment should base on the doctor's judgment on the patient's real-time situation.

8. Which treatment modes and machines to conduct HA330/HA380 hemoperfusion for COVID-19 patients are better?

Both HA330/HA380 are compatible with various blood purification devices, such as CRRT or ECMO. HA330/HA380 hemoperfusion can be connected with HD, HDF, SLED, CVVH, and ECMO for COVID-19 patients. On which modes to select depend on the patients' clinical situation and the medical resource. For example, doctors in the Nephrology Department show higher tendency to combine HA330/HA380 hemoperfusion with HD, HDF, SLED, while those in the ICU is more likely to conduct HA330/HA380 hemoperfusion with CVVH or VV-ECMO, or just single hemoperfusion on a hemoperfusion machine.

9. Is hybrid treatment combining hemoperfusion with CVVH better than single hemoperfusion?

In one hand, the HA330/HA380 hemoperfusion is aimed to absorb excessive cytokine to reduce cytokine storm, regulate body immunity and hemodynamics, but it cannot regulate water-electrolyte, acid-base balance; in another hand, CVVH is inefficient to clear cytokines but effective to clear water-soluble and low protein substances, correct water-electrolyte imbalance. Thus, to combine hemoperfusion with CVVH is better for COVID-19 patients who show the indication needed CRRT, which we can found some proof from the Iran experience of Prof. SM. Reza Hashemian from the webinar.

10. How to choose anticoagulant for hemoperfusion therapy?

Anticoagulants for COVID-19 patients can be heparin, citrate and others such as argatroban. For patients under hyper-coagulation situation, heparin seems to be a favored option.

11. Does plasma concentration of drugs changed during the hemoperfusion therapy?

Yes, just like CRRT therapy, conduct hemoperfusion will decrease some drugs' concentration from the plasma, especially drugs with the organic ring structure without excessive molecular weight. In this way, conducting hemoperfusion avoiding the peak of blood concentration of drugs such as antibiotic and adding the dosage are both viable options we recommend. According to lab data, HA330/HA380 can adsorb around 20-40% of the drugs from vitro, but in vivo especially in critical illness, microcirculation disorder is common seem that the distribution of drugs would be lower. We clinically recommend adding 20% dosage of antibiotic while conduct HP, or if possible, adjusting the drug dosage according to the drug concentration in blood/plasma is ok.

12. Do you experience decreasing platelet count during hemoperfusion therapy?

Not really, but if platelet count drops within 10%, it's acceptable and usually the platelet count would return back to normal later in 1-2 or several days. But if the patient's platelet count is below 60, HP should be better conducted until the platelet level increased above the limit.

13. For patient receiving Tocilizumab, when will hemoperfusion be conducted?

Some doctors are willing to prescribe Tocilizumab in the early stage while IL-6 or CRP elevate, but when the patient shows tendency of AKI or requiring extracorporeal organ support, it's time for hemoperfusion to take control of the cytokine storm. If doctors insist to prescribe Tocilizumab at the same time, don't worry that hemoperfusion will adsorb it because of Tocilizumab has a very large molecular weight over the adsorption range of HA330/HA380.

The webinar video is available on YouTube: <https://www.youtube.com/watch?v=ZzndPUHHOzM>

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