Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Does adjunctive hemoadsorption with CytoSorb affect survival of COVID-19 patients on ECMO? A critical statement

Dear Editor

In addition to the comments of Putzu and Schorer [1] concerning the critical use of hemoadsorption in septic shock, we would like to bring some additional aspects into focus of the discussion surrounding the article by Supady and colleagues on cytokine adsorption in patients with severe COVID-19pneumonia requiring extracorporeal membrane oxygenation (ECMO) [2]. In a randomized controlled trial with 34 patients, the authors interpreted their data in a way that early initiation of cytokine adsorption had a negative effect on survival.

Interleukin 6 (IL6) appears to be a poor marker for follow-up assessment of hyperinflammation progression in CytoSorb-treatment [3] IL6-levels depend on the balance between production, natural depletion, and extracorporeal removal. IL6 decrease may therefore be a major function of the first two mechanisms rather than removal, making it unsuitable as a marker of effectiveness of hemoadsorption. It should be noted that despite the lack of IL6-differences between groups vasopressor support and fluid load were significantly higher in the CytoSorb-group [2].

Effective blockade of the IL6-pathway by tocilizumab may lead to improved outcome during the course of COVID-19 [4,5]. Thus, a relevant inflammatory component in the pathophysiology of COVID-19-pneumonia can be assumed. IL6-levels and vasopressor support reported by Supady and colleagues [2] do not suggest clinically relevant hyperinflammation.

It seems implausible that CytoSorb should be the only difference in treatment between the groups. There is a bias to the disadvantage of the CytoSorb-group that is consistent through all parameters and does not follow normal distribution. The CytoSorb-patients had higher peak-pressures, higher tidal volumes (absolute and per kg) and higher lactate suggesting that the control group had received a more protective ventilation. Comparison of the reported values with registry data [6] shows that in addition to the longer duration of ventilation before ECMO initiation (4.0 vs.5.0d) the P/F-ratio in the CytoSorb-group was clearly lower than the international median (62.7 mmHg vs.72 mmHg) while it was higher in the control group (84.2 mmHg) at the time of ECMO initiation. Thus, treatment differences between the groups cannot be excluded with certainty and could help explain the higher mortality in the CytoSorb-group.

A pathophysiologically based indication for CytoSorb-use is hyperinflammation with multi-organ dysfunction characterized by Sequential-Organ-Failure-Assessment-score (SOFA). The inclusion criteria allowed to include a study population with a SOFA of 9 and thereby CytoSorb use without a strong indication [3]. This might be a reason for a missing positive effect. Also, blood flow rates varied between 100 and 700 ml/min and the total amount-of-blood-purified (ABP) [3] was not mentioned. It remains unclear how much ABP the patients received. No mention is given of the ratio of blood flow through the membrane oxygenator to the adsorber, which could have also created problematic constellations.

The large difference in mortality is of concern to any clinician wishing to use hemoadsorption. Taken together, the uncertainties regarding equality of study groups as well as timing, dosing, and application of supportive sepsis-treatment should cause careful interpretation of the study data and prevent precipitous conclusions. We agree with Putzu and Schorer [1] that only further randomized studies can finally clarify the role of hemoadsorption in the treatment of critically ill patients.

Declaration of Competing Interest

TK has received lecture fees from Cytosorbent Europe. The Department of Anesthesiology at Klinikum Herford has received an unrestricted grant from Cytosorbent Europe in 2018. The authors declare that they have no other competing interests.

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