Interim-analysis of the COSA (COVID-19 Patients Treated With the Seraph® 100 Microbind® Affinity Filter) Registry

Julius J. Schmidt  
Hannover Medical School: Medizinische Hochschule Hannover

Dan Nicolae Borchina  
Städtisches Klinikum Braunschweig GmbH: Stadtsches Klinikum Braunschweig gGmbH

Mariet van’t Klooster  
Klinikum Region Hannover GmbH

Khalida Soki  
Nairobi Hospital

Reuben Okioma  
Nairobi Hospital

Larissa Herbst  
Erlangen University Hospital: Universitätsklinikum Erlangen

Diego Sandoval Rodríguez  
Hospital Universitari de Bellvitge

Stefan Büttner  
Klinikum Aschaffenburg-Alzenau Standort Aschaffenburg: Klinikum Aschaffenburg-Alzenau

Birgit Bader  
Sankt Josef Krankenhaus

Wojciech Serednicki  
University Hospital in Krakow: Szpital Uniwersytecki w Krakowie

Ewa Zasada  
Jagiellonian University: Uniwersytet Jagiellonski w Krakowie

Michael Schmitz  
Städtisches Klinikum Solingen: Stadtsches Klinikum Solingen

Ralf Alexander Quabach  
Städtisches Klinikum Solingen: Stadtsches Klinikum Solingen

Thomas Fühner  
Klinikum Region Hannover GmbH

Jan T Kielstein  
Academic Teaching Hospital Braunschweig  
https://orcid.org/0000-0001-8110-9064
Abstract

Background:

The Seraph®100 Microbind Affinity Blood Filter® is a hemofiltration device that is licensed for pathogen reduction in the blood. This includes several viruses. Removal of the nucleocapsid of the SARS-CoV-2 virus by the Seraph®100 has been recently demonstrated. As viral load has repeatedly been shown to correlate with adverse outcome in severe coronavirus disease 2019 (COVID-19), the aim of this registry was to evaluate safety and efficacy of Seraph®100 treatment for COVID-19.

Methods:

An online registry in which main patient characteristics, treatment coordinates and outcome parameters was documented without reimbursement. So far 12 hospitals in 4 countries on 2 continents took part in the registry. 75 treatment sessions in 60 patients were documented in the registry.

Results:

Adverse effects of the Seraph®100 treatment were reported in 2 (2.6 %) of the 75 treatments. Eight (10.6 %) of all the procedures ended prematurely due to circuit failure / clotting. Half of the treatments (47.6 %) were performed as hemoperfusion only. 21.6 % of the treatments were performed in conjunction with intermittent hemodialysis. Median treatment time was 4.21 [4.00 - 8.06] h. Anticoagulation was performed using citrate in 20.6 % of treatments. Patients that died despite treatment with the Seraph®100 filter had a higher rate of bacterial superinfection, higher level of inflammatory laboratory markers (procalcitonin and ferritin) and higher d-dimer levels. While predicted survival rate in ICU patients was >80 %, the observed survival rate was 47.6 %. In non-ICU patients, 4 C score predicted a survival rate of 31.4-34.9 % while the observed survival rate was 22.2 %.

Conclusion:

Seraph® 100 treatment was well tolerated and circuit failure rate was significantly lower than reported for KRT in COVID-19 patients. All patients that died despite of Seraph® 100 treatment had serious pre-existing medical conditions, coexisting bacterial infections and more pronounced systemic signs of inflammation. Compared to the calculated mortality using established scores, the observed mortality in the Seraph® 100 treated patients was lower.

Trial registration:

ClinicalTrials.gov Identifier: NCT04361500

Introduction
For over a year, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) has a serious impact on health and economics worldwide. Despite the recent advent of SARS-CoV-2 vaccines, treatment options for critically ill patients will be needed. However, pharmacological interventions remain limited. Aside from dexamethasone and encouraging preliminary data using recombinant interleukin-1 receptor antagonist, none of the many repurposed drugs that had been suggested for the treatment of COVID-19 has substantiated its therapeutic effectiveness in randomized prospective trials. With this background, several extracorporeal treatments are currently being explored for their potential to improve clinical course and outcome of critically ill COVID-19 patients. Extracorporeal interventions could eliminate the virus, thereby blunt the immune response to avoid manifestations such as cytokine storm and multiorgan failure. Furthermore, they could ameliorate hypercoagulation and clot formation resulting in venous, arterial and microvascular thrombosis. The evidence supporting the use of extracorporeal devices is neither substantial nor homogenous. Most interventions aim to reduce the cytokine storm although its contribution to COVID-19-induced organ dysfunction as been questioned. Also the effect of therapeutic plasma exchange has previously been doubted, yet using fresh frozen plasma could optimize the vWF/ADMATS-13 ratio. The Seraph® 100 Microbind® Affinity filter (ExThera Medical, Martinez, CA, USA) has recently been introduced for the elimination of bacteria and other pathogens from blood. Authorization for emergency use in patients with COVID-19 admitted to the ICU with confirmed or imminent respiratory failure was granted by the United States Food and Drug Administration. Motivation for approval was the fact that a majority of critically ill patients showed viral RNAemia, which was related to disease severity. This has recently confirmed in a meta-analysis of 21 studies containing 2181 patients. RNAemia was associated with COVID-19 severity with OR of 5.43. In addition, SARS-CoV-2 RNAemia was a significant risk factor for unfavorable clinical outcome, including ICU admission and mortality. Furthermore, RNAemia was also a significant risk factor for invasive mechanical ventilation and multiple organ failure. As the SARS-CoV-2 spike glycoprotein binds tightly to immobilized heparin, the functional backbone of the Seraph® 100, it could decrease RNAemia. Recently it had been shown that Seraph® 100 Microbind® Affinity filter removes the nucleocapsid protein of SARS-CoV-2 in critically ill COVID-19 patients. Here we report the interim analysis of the COVID-19 patients treated with the Seraph® 100 Microbind® Affinity filter (COSA) registry.

Patients And Methods

The registry for the Evaluation of Safety and Effectiveness of the Seraph 100® Microbind Affinity Blood Filter in the Therapy of COVID-19 Patients (COSA) had been registred in ClinicalTrials.gov Identifier: NCT04361500).

The registry was initially approved by the Institutional Review Board of the Hannover Medical School. Currently 12 hospitals from four countries on two continents contributed to the registry. Data entry was not reimbursed.
Results

Of the 75 entered datasheets in the registry, 15 represented multiple treatments in single patients (Figure 1). After exclusion of incompletely documented patients, partly due to ongoing ICU treatment, 51 patients could be analyzed. Upon analysis of the entire cohort, the deceased population showed a higher incidence of bacterial infections (66.7 % vs. 21.7 %; p=0.007) and inflammatory markers, such as procalcitonin (p=0.012) and ferritin (p=0.014). Furthermore, higher d-dimer levels at the start of treatment were seen in patients that did not survive. Body weight and height as well as age in the patients that deceased was not different from surviving patients (Table 1). In the ICU patient cohort (n=42), Seraph® treatment was initiated earlier after symptom onset (8.51 [5.6 - 12.1] days) in surviving patients (p=0.032) (Table 2).

While predicted mortality rate based on the SOFA score in ICU patients was >80 % [18], the observed mortality rate was 47.6%. In non-ICU patients, 4C mortality score for COVID-19 predicted a mortality rate of 31.4-34.9% [19] while the observed mortality rate was 22.2%.

Circuit failure was the most common adverse event, occurring in 10.6 % of the patients (Table 3).

Discussion

To our knowledge this report describes the largest cohort of critically ill patients with COVID-19 treated with the Seraph®100 Microbind® Affinity apart from case studies [20-22] and a recently pre-print published US-cohort [23].

The Seraph®100 filter has been licensed in the European Union in 2019 for the removal of pathogens from blood. The functional basis of the device are ultra-high molecular weight polyethylene beads with endpoint-attached heparin. Bacteria, viruses, fungi and toxins have been shown to bind to the immobilized heparin in a similar way to the interaction with heparan sulfate on the cell-surface [14]. Due to this biomimetic action pathogens binds irreversibly to the heparin on the polyethylene beads and are thereby removed from the bloodstream. Indeed, recent data have shown that the Seraph® 100 Microbind® Affinity filter removes the nucleocapsid protein of SARS-CoV-2 and might therefore improve the clinical course of critically ill COVID-19 patients in whom viremia correlates and predicts adverse outcome. This comes to no surprise, as heparin-binding is a frequent feature in viruses. This ability is important to bind heparan sulfate proteoglycans on the surface of host cells – a precondition to enter the cells through internalization. For SARS-CoV-2 it has been shown that it not only binds to heparin but also that ACE2-mediated coronavirus entry can be mitigated by heparin, a heparan sulfate-related glycan, or by genetic ablation of biosynthetic enzymes for the cell surface heparan sulfate proteoglycans [24].

Mortality in the COSA registry

The mortality of 42.3 % in our entire cohort is comparable with the 38% mortality in the Purify OBS study [23] even though more patients in the COSA registry were treated by mechanical ventilation (66.7 % vs
56.6 %). The observed survival rate in both the ICU patients and the non-ICU patients was lower than predicted by the SOFA score [18] or the 4C score [19] respectively. These differences have to be carefully judged in the light of the fact that the data comes from a registry.

**Mortality and inflammation**

Most of the laboratory differences between the patients that survived and those that succumbed were related to inflammation. Early reports from China already showed that a fulminant inflammatory response to the viral infection correlates with disease severity [25]. Hence the discriminating variables in our cohort is in line with published data.

**Low rate of circuit failure**

A single center analysis showed that >30% hemofilters failed within 9 hours due to clotting. The median circuit life was 21 hours [26]. In our analysis filter clotting was as low as 10.6 %, although almost half of the treatments were performed in conjunction with renal replacement therapy.

**Study Limitations**

The inherent limitation of a registry study in comparison to a prospective randomized trial is the lack of a control group. Nonetheless, the collection of data will help to focus future prospective randomized trials in terms of inclusion / exclusion criteria as well as variables investigated. Ongoing prospective clinical trials in Europe (NCT04547257) and the US (NCT04606498) will clarify the role of the Seraph® 100 filter in the treatment of critically ill COVID-19 patients.

**Conclusions**

Treatment of critically ill patients with the Seraph® 100 filter has been shown to be well tolerated. It is associated with a low clotting rate. Furthermore, the observed mortality is lower in comparison to the predicted mortality. This has to be carefully interpreted in the light of the inherent limitations of a registry.

**Declarations**

**Ethical approval:**

This study was approved by the Ethics Committee of the Hannover Medical School as well as the respective Ethics Committees of the participating institutions.

**Consent for publication:**

Not applicable.

**Availability of data and materials:**
The datasets of the current study are available from the corresponding author on reasonable request.

**Competing interests:**

Stefan Büttner, Thomas Fühner, Jan T. Kielstein and Julius J. Schmidt received research support from ExThera Medical.

**Funding:**

Infrastructural and IT support came from GORTA, Ireland’s longest-running international development organization. They had neither an influence on the design of the study nor on data collection, analysis, and interpretation of data or the writing and content of the manuscript.

**Authors’ contributions:**

JS and JK designed the study and applied for the initial IRB approval. JS, JK, DB and TF analyzed the data, designed the figures and wrote the initial draft of the manuscript. MK did all the English language corrections. Sequence of authorship was related to the number of the recruited patients per center. All centres recruiting more than 5 patients have two authors on the manuscript. All authors read and approved the final manuscript.

**Acknowledgements:**

We thank Ms. Alina Siegert for her logistical support.

**References**

1. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Perez Marc G, Moreira ED, Zerbini C et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020.

2. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2020.

3. Group RC, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A et al. Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report. *N Engl J Med* 2020.

4. Kooistra EJ, Waalders NJB, Grondman I, Janssen NAF, de Nooijer AH, Netea MG, van de Veerdonk FL, Ewalds E, van der Hoeven JG, Kox M et al. Anakinra treatment in critically ill COVID-19 patients: a prospective cohort study. *Crit Care* 2020, 24(1):688.

5. Rosas IO, Brau N, Waters M, Go RC, Hunter BD, Bhagani S, Skiest D, Aziz MS, Cooper N, Douglas IS et al. Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia. *N Engl J Med* 2021.

6. Salama C, Han J, Yau L, Reiss WG, Kramer B, Neidhart JD, Criner GJ, Kaplan-Lewis E, Baden R, Pandit L et al. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. *N Engl J Med* 2020.
7. Consortium WHOST, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, Abdool Karim Q, Alejandria MM, Hernandez Garcia C, Kieny MP et al: Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results. 2020.

8. Group RC, Horby P, Mafham M, Linsell L, Bell JL, Staplin N, Emberson JR, Wiselka M, Ustianowski A, Elmahi E et al: Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19. N Engl J Med 2020, 383(21):2030-2040.

9. Ronco C, Reis T: Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol 2020.

10. Leisman DE, Ronner L, Pinotti R, Taylor MD, Sinha P, Calfee CS, Hirayama AV, Mastroiani F, Turtle CJ, Harhay MO et al: Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes. Lancet Respir Med 2020, 8(12):1233-1244.

11. Honore PM, Barreto Gutierrez L, Kugener L, Redant S, Attou R, Gallerani A, De Bels D: Plasma exchange in critically ill COVID-19 patients improved inflammation, microcirculatory clot formation, and hypotension, thereby improving clinical outcomes: fact or fiction? Crit Care 2020, 24(1):551.

12. Doevelaar AAN, Bachmann M, Holzer B, Seibert FS, Rohn BJ, Bauer F, Witzke O, Dittmer U, Bachmann M, Yilmaz S et al: von Willebrand Factor Multimer Formation Contributes to Immunothrombosis in Coronavirus Disease 2019. Crit Care Med 2021.

13. Seffer MT, Eden G, Engelmann S, Kielstein JT: Elimination of Staphylococcus aureus from the bloodstream using a novel biomimetic sorbent haemoperfusion device. BMJ Case Rep 2020, 13(8).

14. Seffer MT, Cottam D, Forni LG, Kielstein JT: Heparin 2.0: A New Approach to the Infection Crisis. Blood Purif 2020:1-7.

15. Bermejo-Martin JF, Gonzalez-Rivera M, Almansa R, Micheloud D, Tedim AP, Dominguez-Gil M, Resino S, Martin-Fernandez M, Ryan Murua P, Perez-Garcia F et al: Viral RNA load in plasma is associated with critical illness and a dysregulated host response in COVID-19. Crit Care 2020, 24(1):691.

16. Tang K, Wu L, Luo Y, Gong B: Quantitative assessment of SARS-CoV-2 RNAemia and outcome in patients with Coronavirus Disease 2019. J Med Virol 2021.

17. Kim SY, Jin W, Sood A, Montgomery DW, Grant OC, Fuster MM, Fu L, Dordick JS, Woods RJ, Zhang F et al: Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. Antiviral Res 2020, 181:104873.

18. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL: Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 2001, 286(14):1754-1758.

19. Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, Dunning J, Fairfield CJ, Gamble C, Green CA et al: Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ 2020, 370:m3339.

20. Olson SW, Oliver JD, Collen J, Bunin J, Gleeson TD, Foster BE, Simmons MP, Chen HW, Ficke JB, Brown TE et al: Treatment for Severe Coronavirus Disease 2019 With the Seraph-100 Microbind
21. Pape A, Kielstein JT, Kruger T, Fuhner T, Brunkhorst R: Treatment of a Critically Ill COVID-19 Patient with the Seraph 100 Microbind Affinity Filter. *TH Open* 2021, **5**(2):e134-e138.

22. Sandoval D, Rama I, Quero M, Hueso M, Gomez F, Cruzado JM: Treatment for severe COVID-19 with a biomimetic sorbent haemoperfusion device in patients on haemodialysis. *Clin Kidney J* 2021, **14**(5):1475-1477.

23. A Multicenter Evaluation of Blood Purification with Seraph 100 Microbind Affinity Blood Filter for the Treatment of Severe COVID-19: A Preliminary Report [https://www.medrxiv.org/content/10.1101/2021.04.20.21255810v1]

24. Zhang Q, Chen CZ, Swaroop M, Xu M, Wang L, Lee J, Pradhan M, Shen M, Luo Z, Xu Y et al: Targeting heparan sulfate proteoglycan-assisted endocytosis as a COVID-19 therapeutic option. *bioRxiv* 2020.

25. Zeng Z, Yu H, Chen H, Qi W, Chen L, Chen G, Yan W, Chen T, Ning Q, Han M et al: Longitudinal changes of inflammatory parameters and their correlation with disease severity and outcomes in patients with COVID-19 from Wuhan, China. *Crit Care* 2020, **24**(1):525.

26. Shankaranarayanan D, Muthukumar T, Barbar T, Bhasin A, Gerardine S, Lamba P, Leuprecht L, Neupane SP, Salinas T, Shimonov D et al: Anticoagulation Strategies and Filter Life in COVID-19 Patients Receiving Continuous Renal Replacement Therapy: A Single-Center Experience. *Clin J Am Soc Nephrol* 2020, **16**(1):124-126.

Tables

**Table 1**: Characteristics of all included patients, stratified for survival. Data are presented as median and interquartile range [IQR] unless otherwise stated.
|                                | Overall | Non-Survivor | Survivor | p  |
|--------------------------------|---------|--------------|----------|----|
| n                              | 51      | 22           | 29       |    |
| Mortality (%)                  | 42.3%   |              |          |    |
| Age (years)                    | 63.00   | 64.00        | 57.00    | 0.156|
|                                | [54.00 - 69.50] | [57.75 - 71.75] | [52.00 - 68.00] |    |
| Sex = Male (%)                 | 40 (78.4) | 17 (77.3)    | 23 (79.3) | 1   |
| White                          | 40 (83.3) | 17 (81.0)    | 23 (85.2) | 0.707|
| Weight (kg)                    | 90 [79 - 111] | 90 [80.25 - 103.50] | 90 [79 - 116] | 0.974|
| Height (cm)                    | 175.00 [170.00 - 180.00] | 173.00 [170.00 - 181.00] | 175.00 [173.00 - 179.00] | 0.695|
| SOFA Score                     | 11.50 [9.00 - 14.00] | 13.00 [9.00 - 15.00] | 11.00 [8.00 - 13.00] | 0.129|
| 4C-Score                       | 12.00 [9.25 - 13.75] | 12.00 [11.00 - 14.00] | 10.50 [8.00 - 12.00] | 0.038|
| Hemodynamic stability (%)      |         |              |          | 0.131|
| Dopamine < 5 OR DOBUTamine (any dose) | 2 (4.2) | 1 (5.0)      | 1 (3.6)  |    |
| Dopamine > 15 OR EPINEPHrine > 0.1 OR norEPINEPHrine > 0.1 | 12 (25.0) | 4 (20.0)     | 8 (28.6) |    |
| Dopamine > 5 OR EPINEPHrine < 0.1 OR norEPINEPHrine < 0.1 | 12 (25.0) | 7 (35.0)     | 5 (17.9) |    |
| MAP < 70 mmHg                  | 5 (10.4) | 4 (20.0)     | 1 (3.6)  |    |
| No hypotension                 | 17 (35.4) | 4 (20.0)     | 13 (46.4) |    |
| Invasive ventilation (%)       | 34 (66.7) | 16 (72.7)    | 18 (62.1) | 0.617|
| PaO₂/FIO₂                      | 149.62   | 151.25       | 148.00   | 0.391|
|                              | [110.57 - 176.88] | [121.67 - 177.50] | [82.80 - 171.11] | p     |
|------------------------------|-------------------|-------------------|-------------------|-------|
| **Bacterial superinfection, n (%)** | 19 (43.2)         | 14 (66.7)         | 5 (21.7)          | **0.007** |
| **CRP (mg/L)**               | 129.00            | 127.00            | 132.50            | 0.928 |
|                              | [87.00 - 244.00]  | [65.00 - 319.00]  | [107.25 - 217.75] |
| **PCT (µg/L)**               | 1.00              | 3.55              | 0.60              | **0.012** |
|                              | [0.45 - 4.85]     | [0.85 - 7.55]     | [0.30 - 1.50]     |
| **Leukocytes (x1000/µL)**    | 9.90              | 11.30             | 9.30              | 0.419 |
|                              | [7.30 - 14.70]    | [8.03 - 14.45]    | [7.10 - 14.80]    |
| **Ferritin (ng/mL)**         | 1258.50           | 2425.50           | 987.00            | **0.014** |
|                              | [825.50 - 2212.75]| [1478.25 - 7021.50]| [675.00 - 1818.00]|
| **Troponin-T (pg/mL)**       | 26.50             | 60.00             | 24.00             | 0.656 |
|                              | [13.50 - 95.00]   | [16.00 - 98.00]   | [13.00 - 76.50]   |
| **NT-proBNP (ng/µL)**        | 775.00            | 2087.00           | 589.00            | 0.063 |
|                              | [395.00 - 2470.00]| [888.25 - 9483.75]| [342.00 - 1114.50]|
| **D-Dimer (mg/L)**           | 2.82              | 4.60              | 1.58              | **0.039** |
|                              | [1.03 - 11.56]    | [1.89 - 18.67]    | [0.74 - 5.50]     |
| **Onset of symptoms to Seraph treatment (d)** | 10.38             | 11.58             | 9.13              | 0.118 |
|                              | [6.57 - 14.19]    | [8.57 - 16.00]    | [5.85 - 13.55]    |
| **ICU admission to Seraph treatment (d)** | 2.31              | 2.58              | 1.77              | 0.158 |
|                              | [1.51 - 4.28]     | [1.62 - 5.57]     | [1.49 - 3.28]     |
| **Treated blood volume (L)**  | 75.75             | 92.80             | 66.50             | 0.060 |
|                              | [60.00 - 132.75]  | [66.62 - 195.45]  | [60.00 - 77.81]   |
| Treatment                          | n (%)   | n (%)   | n (%)   | p-value |
|-----------------------------------|---------|---------|---------|---------|
| Seraph as stand alone treatment, n(%) | 30 (47.6) | 6 (28.6) | 25 (50) | 0.022   |
| Kidney Replacement Therapy, n (%)  | 19 (38.8) | 8 (40.0) | 11 (37.9) | 1       |
| Intermittent hemodialysis, n (%)   | 11 (21.6) | 3 (13.6) | 8 (27.6) | 0.392   |
| ECMO treatment, n (%)              | 5 (9.8)  | 4 (18.2) | 1 (3.4)  | 0.202   |

**Table 2:** Patient characteristics of ICU patients. Stratified for survival. Data are presented as median and interquartile range [IQR] unless otherwise stated.
|                                | Overall | Non-Survivor | Survivor | p     |
|--------------------------------|---------|--------------|----------|-------|
| n                              | 42      | 20           | 22       |       |
| Mortality (%)                  | 47.6 %  |              |          |       |
| Age in years (median [IQR])    | 60.50   | 64.00        | 55.50    | 0.066 |
|                                | [53.25 - 68.00] | [56.50 - 70.25] | [49.75 - 66.50] |       |
| Sex = Male (%)                 | 33 (78.6) | 15 (75.0)  | 18 (81.8) | 0.872 |
| White                          | 31 (79.5) | 15 (78.9)  | 16 (80.0) | 0.763 |
| Weight (kg)                    | 90 [80 - 113] | 96 [84 - 107] | 90 [80 - 115] | 0.988 |
| Height (cm)                    | 175.00 [172.50 - 180.00] | 173.00 [170.00 - 182.00] | 177.00 [175.00 - 178.75] | 0.426 |
| SOFA Score                     | 12.00 [9.00 - 14.00] | 13.50 [10.50 - 15.00] | 11.00 [9.00 - 13.75] | 0.197 |
| 4C-Score                       | 12.00 [9.00 - 14.00] | 12.00 [11.00 - 14.00] | 10.00 [8.00 - 12.00] | 0.063 |
| Hemodynamic stability (%)      |         |              |          | 0.194 |
| Dopamine < 5 OR DOBUTamine (any dose) | 2 (5.1) | 1 (5.6) | 1 (4.8) |
| Dopamine > 15 OR EPINEPHrine > 0.1 OR norEPINEPHrine > 0.1 | 12 (30.8) | 4 (22.2) | 8 (38.1) |
| Dopamine > 5 OR EPINEPHrine < 0.1 OR norEPINEPHrine < 0.1 | 12 (30.8) | 7 (38.9) | 5 (23.8) |
| MAP < 70 mmHg                  | 3 (7.7)  | 3 (16.7)     | 0 (0.0)  |       |
| No hypotension, n (%)          | 10 (25.6) | 3 (16.7) | 7 (33.3) |       |
| Invasive ventilation, n (%)    | 34 (81.0) | 16 (80.0) | 18 (81.8) | 1     |
| PaO2/FIO2                      | 146.00  | 148.62       | 132.50   | 0.425 |
|                          | [109.33 - 173.85] | [118.58 - 175.62] | [82.80 - 171.11] |
|--------------------------|-------------------|-------------------|------------------|
| **Bacterial superinfection, n (%)** | 17 (45.9) | 13 (68.4) | 4 (22.2) | **0.013** |
| **CRP (mg/L)**           | 142.00           | 150.00           | 141.00           | 0.935 |
|                          | [96.75 - 276.00] | [76.00 - 331.50] | [114.00 - 230.00] |
| **PCT (µg/L)**           | 1.45             | 4.20             | 0.60             | 0.063 |
|                          | [0.50 - 6.12]    | [0.95 - 8.50]    | [0.43 - 3.08]    |
| **Leukocytes (x1000/µL)**| 11.30            | 12.65            | 10.95            | 0.99 |
|                          | [7.70 - 14.80]   | [7.90 - 14.65]   | [7.60 - 16.25]   |
| **Ferritin (ng/mL)**     | 1342.00          | 2425.50          | 1111.50          | 0.051 |
|                          | [914.00 - 2212.75] | [1266.50 - 8340.50] | [868.50 - 2000.00] |
| **Troponin-T (pg/mL)**   | 24.00            | 23.00            | 26.50            | 0.805 |
|                          | [12.00 - 81.00]  | [14.00 - 99.00]  | [12.75 - 69.00]  |
| **NT-proBNP (ng/µL)**    | 905.00           | 2087.00          | 621.00           | 0.074 |
|                          | [457.00 - 2488.50] | [888.25 - 9483.75] | [345.00 - 1154.25] |
| **D-Dimer (mg/L)**       | 3.90             | 4.60             | 2.00             | 0.202 |
|                          | [1.27 - 20.50]   | [1.80 - 22.34]   | [0.79 - 11.36]   |
| **Onset of symptoms to Seraph treatment (d)** | 10.19 | 12.12 | 8.51 | **0.032** |
|                          | [6.53 - 14.33]   | [9.28 - 17.32]   | [5.60 - 12.15]   |
| **ICU admission to Seraph treatment (d)** | 2.31 | 2.58 | 1.77 | 0.158 |
|                          | [1.51 - 4.28]    | [1.62 - 5.57]    | [1.49 - 3.28]    |
| **Kidney replacement therapy, n (%)** | 13 (32.5) | 6 (33.3) | 7 (31.8) | 1 |
| **ECMO treatment, n (%)** | 5 (11.9) | 4 (20.0) | 1 (4.5) | 0.286 |
Table 3: Reported treatment characteristics, adverse events and system failures.

|                                |       |
|--------------------------------|-------|
| **Total number of treatments, n** | 75    |
| **Seraph treatment time in h [IQR]** | 4.21 [4.00, 8.06] |
| **Seraph blood flow in mL/min [IQR]** | 200 [110, 250] |

**Anticoagulation**

- **Heparin, n (%)** | 38 (50.7 %)
- **Citrate, n (%)** | 15 (20 %)
- **Hypotension, n (%)** | 2 (2.7 %)

**Adverse events documented, n (%)** | 8 (10.6 %)

**Clotting events, n (%)** | 8 (10.6 %)

**Shivering, n (%)** | 1 (1.3 %)

Figures
Figure 1

CONSORT diagram of included patients.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CritCareCOSAvisualabstract.pdf