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Letter to Editor

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A Rare Case of Successful Multiple Prolonged Runs of Extracorporeal Life Support for Severe Covid-19-Related Acute Respiratory Distress Syndrome

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Editorial

Extracorporeal life support (ECLS) is used worldwide as rescue therapy to manage severe COVID-19-related acute respiratory distress syndrome (ARDS). In patients supported with venovenous extracorporeal membrane oxygenation (VV ECMO) for COVID-19-related ARDS, the overall mortality rate is approximately 39%, and the mean ECMO duration (approximately 15 days) seems to be longer than that of other etiologies [1]. Only a few cases of successful native lung recovery have been reported after prolonged VV ECMO (>28 days) [2,3]. Data on multiple runs of VV-ECMO are limited and refer to the period before COVID-19. Until 2015, the survival-to-discharge rate of patients requiring multiple VV ECMO runs had decreased for each subsequent run [4].

We report a rare case of successful lung recovery after almost six months of ECLS in a patient with severe COVID-19-related ARDS complicated by bacterial and fungal septic shock requiring multiple extracorporeal treatment runs. The patient provided written informed consent for the publication of this case report.

In December 2021, a 44 years old Caucasian male patient without comorbidities was hospitalized for acute respiratory failure after five days of fever. The nasopharyngeal swab was positive for SARS-CoV-2. The computed tomography (CT) scan revealed bilateral tree-in-bud opacities and parenchymal consolidations, allowing the diagnosis of COVID-19-related ARDS. After two weeks of Noninvasive Mechanical Ventilation (NIMV) and pharmacological therapy with tocilizumab, remdesivir, and casirivimab without benefits, he was intubated. Despite high positive end-expiratory pressure (PEEP), inhaled nitric oxide (iNO), continuous infusion of neuromuscular blockade agents, and six prone position cycles, he progressively developed a reduction of lung static compliance (Cstat 30 ml cmH2O-1) and severe hypercapnic respiratory failure (pH 7.2, PaCO2 90 mmHg, PaO2/FiO2 170). After 12 days, he was referred to our centre for VV ECMO. Despite the days of mechanical ventilation, in consideration of the young age, the lack of comorbidities, and the absence of superinfection or another organ failure, we decided to start VV ECMO. After one month, he developed a bacterial pulmonary superinfection caused by multidrug resistance (MDR) Pseudomonas aeruginosa. On day 76, he was weaned from ECMO.

After four days, the patient developed severe refractory hypoxia resulting in seizures and a severe septic shock requiring high doses of norepinephrine and terlipressin. We performed an urgent full-body CT scan that documented a complete subversion of the lung architecture and we prescribed an empirical antimicrobial therapy with meropenem and caspofungin. We contacted the referral centre for a lung transplant. Meanwhile, considering the critical conditions and the young age, we decided to perform a second

run of VV ECMO. After the results of blood cultures, positive for Saccharomyces cerevisiae, Candida parapsilosis, and Ralstonia insidiosa, the lung transplant was contraindicated. We started a combination therapy with ceftazidime-avibactam and fosfomycin for recurrent ventilatory-associated pneumonia (VAP) from MDR Pseudomonas aeruginosa. During this period, the patient followed a nutritional, endocrinological, neurorehabilitative, and psychological program. The blood cultures became negative for Candida parapsilosis after three months of antifungal combination therapy with caspofungin and amphotericin. On day 78 of the second run, the ECLS was discontinued.

After six months in the intensive care unit (ICU), the patient was referred to the general ward. Twenty days later, he developed dyspnea and bronchospasm. A CT tomography showed recurrence of peripheral lung consolidations. The patient was readmitted to our ICU, intubated, and treated with continuous neuromuscular blockade, iNO, and sevoflurane. We diagnosed septic shock caused by Enterococcus faecalis and Pseudomonas aeruginosa, which was treated with antimicrobial therapy with cefiderocol, vancomycin, high doses of vasopressors, and levosimendan. Continuous renal replacement therapy with extracorporeal CO2 removal (ECCO2R) was initiated for severe hypercapnia (PaCO2 97 mmHg) associated with anuria. On day 11, the patient's clinical condition improved and extracorporeal treatment was discontinued. A surgical tracheostomy was performed, and the patient was gradually weaned off the ventilator. In September 2022, after nine months of hospitalization, the patient was transferred to a rehabilitation hospital.

To the best of our knowledge, only a second ECLS run can be considered [4]. Sella et al. described the case of a peripartum patient with COVID-19-related ARDS who was successfully supported with two consecutive runs of VV ECMO [5]. In our case, the patient required multiple prolonged ECLS runs for 165 days. In the literature, an exiguous number of ECLS with similar durations in COVID-19 patients has been reported [3]. In the study by Mohanka et al., a duration > 100 days was associated with poor outcomes or the need for transplantation [3].

Despite the long treatment duration, only minor bleeding and infection occurred in our patient. MDR Pseudomonas aeruginosa caused recurrent VAP, and after the first decannulation, a fungal infection caused septic shock, explaining the requirement for the second ECMO run. The onset of metabolic acidosis decompensated the precarious balance of the lung, and compliance improved before gas exchange. Moreover, during the second run, failure of the weaning trials was mainly due to respiratory acidosis, although the tidal volume returned to normal. Additionally, superinfections contribute to delayed recovery. A recent study reported that prolonged ECMO is a risk factor for candidemia, and bloodstream infections, especially those caused by Candida spp, are associated with poor clinical outcomes [6]. This can be explained by two factors. First, complete source control is inapplicable because cannula replacement is usually challenging. Second, the pharmacokinetic and pharmacodynamic characteristics of most antifungals are altered during ECLS.

In conclusion, in conditions with unclear evolution, such as severe COVID-19-related ARDS, a bridge with prolonged ECLS may allow lung recovery without the need for transplantation. Because the predictive factors for lung recovery and timing are not yet known and ECLS is a resource-intensive therapy with a high risk of complications, accurate and tailored case-by-case evaluation is mandatory. The performance status of the patient before the ICU admission and the absence of organ failure are important factors to consider, but not the only ones.

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