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Extracorporeal Membrane Oxygenation for Critically Ill Patients with COVID-19–related Acute Respiratory Distress Syndrome: Worth the Effort!

To the Editor:

Continuous assessment of therapeutic interventions in clinical practice is of paramount importance, in particular in the field of critical care medicine. Falcoz and colleagues recently published a single-center case series of 16 patients with coronavirus disease (COVID-19) requiring extracorporeal membrane oxygenation (ECMO) for severe refractory respiratory failure (1). Overall mortality was 35% at Day 60. Given the fact that average mortality in severe acute respiratory distress syndrome (ARDS) is reported to be around 45% (2), on the basis of Winston Churchill's aphorism, we see beautiful results but we would like to look at the strategy.

The authors used a dual-lumen cannula (DLC) in 75% of cases (12/16 cannulations). A relatively high rate of bleeding complications is reported (1), and the authors state that they adopted higher anticoagulation targets for all patients than usual, with therapeutic dosing of unfractionated heparin, despite a possible higher risk of bleeding in patients with COVID-19 (3). The use of DLC in this setting might be limited by several factors: First, the blood flow of DLC is regularly generated by high pressures, being traumatic for the blood, which in turn might increase bleeding risk. In addition, the DLC is the only cannula that is not

Originally Published in Press as DOI: 10.1164/rccm.202006-2505LE on August 14, 2020

heparin coated. Thus, higher anticoagulation to avoid thrombosis is needed. Second, large-bore DLC are associated with a higher rate of intracranial bleeding (4) and a relatively high rate of insertion site bleeding (5) in the general ICU population, and these risks might be more accentuated with a more liberal anticoagulation strategy. Considering higher targets of anticoagulation owing to the prothrombotic status associated with COVID-19 (6), one may argue that the cannulation strategy might explain this high bleeding rate. Moreover, the authors did not comment if patients were overanticoagulated at the time of bleeding or report what their transfusion thresholds for red blood cells are, which makes it difficult to judge the severity of blood losses. The notion that patients with COVID-19 on ECMO should be on an adequately higher level of therapeutic anticoagulation than usual is not justified by the presented data.

An advantage of the DLC over conventional cannulation was not used, that is, the higher rate to achieve prone positioning compared with conventional cannulation (7).

The authors further state that they adjusted their ventilation strategy after ECMO implantation. At the time ECMO was implanted, patients were ventilated at parameters that would be in line with recommendations for protective ventilation, except for a high respiratory frequency. Reportedly, only one patient had high P_{CO_2} at the time of cannulation. At the time of ECMO implantation, driving pressure (ΔP) was 15 cm H_2O (range, 7–23 cm H_2O), a value seeming to be a break point for higher mortality in a previous analysis (8). Surprisingly, the authors reduced ΔP in median by 1 cm H_2O only, as positive end-expiratory pressure (PEEP) and plateau pressures were both reduced in a similar manner. During the time of ECMO, ΔP was still close to 15 cm H_2O and the range of driving pressures under ECMO was 8–23 cm H_2O; thus, some patients still had a relatively high ΔP. Hence, an important advantage of ECMO, to reduce ΔP at a constant PEEP and control for CO_2 by sweep-gas flow, was not fully used.

Another relevant aspect, rather neglected in the paper, refers to the strategy of support over time: indeed, it would have been interesting to appreciate whether cardiocirculatory depression occurred in the patients with unfavorable outcome, a condition that has been observed rather frequently in patients with COVID-19. The rate of cardiorespiratory ECMO support in the few published series shows that combined support (venoarterial or venovenoarterial ECMO) was required in less than 10% of the patients, with an even smaller rate observed in the experience of Falcoz and colleagues (only one patient). However, direct myocardial involvement, the development of circulatory shock, and other cardiovascular adverse events, like acute pulmonary embolism despite effective anticoagulation, previously described complications in COVID-19, are partially recorded but not fully explained. Therefore, it would be interesting to know the actual determinants of death in the study. Can the authors speculate if a broader use or conversion to venoarterial or venovenoarterial ECMO in some of these patients would have changed the picture?

It is of utmost importance to try to unambiguously clarify the role of ECMO in acute respiratory distress. ECMO can be part of a useful strategy in ARDS in properly selected patients (9) and if advantages are protected against complications. COVID-19–related ARDS does not make an exemption, and the data presented by Falcoz and colleagues (1) do not support that an exemption has to be made. The reported complications do not appear to be specific for this group of patients and might in part be explained by the ECMO strategy used. As two-thirds of patients in the study recovered, we agree with the authors that venovenous ECMO should be considered as a rescue therapy if conventional ventilation fails—but this is also true for all patients with ARDS. ■

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Reply to Wengenmayer *et al.*

From the Authors:

We read with interest the correspondence from Wengenmayer and colleagues. The authors suggested that we should have adjusted our ventilation strategy under extracorporeal membrane oxygenation (ECMO) to be more protective. As recommended in the Extracorporeal Life Support Organization (ELSO) guidelines (1), we maintained a high positive end-expiratory pressure (PEEP) and reduced V_T to maintain a plateau pressure (PP) under 25 cm H_2O, but we did not drastically reduce the respiratory rate and the driving pressure (ΔP). The measure of these two parameters are indeed associated with mortality at Day 1 of acute respiratory distress syndrome (ARDS) (2) but not the ΔP in patients with obesity (most of our patients) (3). Thus, reducing ΔP by decreasing V_T in patients with obesity could probably not be the main goal when PP remains acceptable. Indeed, the LUNG SAFE (Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure) study (2) did not show any superiority of the ΔP to predict mortality. Furthermore, even if the ΔP value at day 1 was associated with mortality, to date, optimizing this parameter during the following days is not correlated with survival. Knowing the specificity of coronavirus disease (COVID-19)–related ARDS (4) and the high rate of patients with obesity treated in our small cohort (58.8%), one could advance that our strategy might be more protective by preventing overdistension.

Our cannulation strategy is much more a matter of debate: the double-lumen cannulas are indeed not recommended in first intension by ELSO (1) because their positioning can be longer and require the use of an ultrasound system. Regarding oxygenation and decarboxylation, this type of cannula is as efficient as conventional cannulation (5). Our team is experienced in this type of cannulation, limiting the adverse events during cannulation. In view of the morphotype of our patients, a single jugular cannulation facilitated their half-seated position and nursing. Moreover, these cannulas have the advantage of encouraging patient mobilization (5) and potentially limiting the consumption of sedatives, which is not insignificant in the context of a period with work overload. Because this type of cannula is associated with more bleeding (6), we wondered if the high rate of bleeding in our series is facilitated by the cannula, anticoagulation, or the transfusion strategy. Our transfusion target is consistent with ELSO guidelines (1). Concerning the anticoagulation, neither of the two patients with serious hemorrhagic events were overanticoagulated, and the five other patients were transfused on minor bleedings or hemolysis without a negative impact on patient prognosis. On the other hand, we reported two oxygenator thrombosis and three thromboembolic events. Considering the high incidence of thrombotic events in patients with COVID-19 and the ELSO guidelines (1), our anticoagulation target seems to be reasonable.

In our series, two patients died of refractory ARDS with pulmonary fibrosis making the respiratory weaning impossible after decannulation. Two patients developed refractory septic shock with a predominance of vasoplegia, making conversion to venoaterial ECMO (VA-ECMO) ineffective. One patient died during cannulation of cardiac tamponade, and one was on VA-ECMO. Thus, optimizing the support during the time either by converting to VA-ECMO or adding a second cannula would not have modified the mortality of our case series. It is important to note that the context of pandemic-induced work overload and the patients' management by interim intensivists who were not used to taking care of patients with ARDS with ECMO may explain some intensive care management difficulties and suboptimal ventilator settings.

In conclusion, in the context of the pandemic, we have chosen a mastered management of our patients. However, ECMO implantation in refractory ARDS related to COVID-19 allowed more protective ventilation parameters, improving patient status. Our results highlighted a preference for an adaptation of ventilator parameters on the PP and moderate PEEP in this specific series characterized by more obese patients and 65% survival in the ICU. ■

Originally Published in Press as DOI: 10.1164/rccm.202007-2670LE on August 14, 2020