# AN EXTRACORPOREAL MEMBRANE OXYGENATION TREATMENT IN COVID-19 PATIENT – A CASE REPORT FROMSOETOMO HOSPITAL SURABAYA

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## ABSTRACT

COVID-19 patients can experience severe or critical symptoms, which develop into an acute respiratory distress syndrome (ARDS) necessitating an intensive care, of which 80% demanding the mechanical ventilation therapy. Patients with severe and critical infection from COVID-19 can receive Extracorporeal membrane oxygenation (ECMO) therapy. This study reported a successful ECMO therapy at Soetomo Hospital in Surabaya, Indonesia, despite all the problems which occurred during ECMO support especially with coagulation conditions. Thus, an anticoagulant therapy contributed significantly in the success of ECMO therapy.

Keywords: COVID-19, ECMO, Heparin

## INTRODUCTION

The vastly spread of severe acute respiratory syndrome coronavirus (SARS-CoV-2) in China and around the world has led to a global health disaster due to its fast human-to-human infection and strong virulence. There are approximately five to fourteen percent of COVID-19 patients having possibilities in experiencing severe or critical symptoms, which are able to develop into an acute respiratory distress syndrome (ARDS) necessitating a treatment intensively, of which 80% of them are in need of mechanical ventilation therapy (1).

Severe COVID-19 patients receive antibiotic therapy, antiviral, anticoagulant, corticosteroid, vitamin C, vitamin D and treatment according to comorbidities and complications. The severe and critical COVID-19 patients have the probabilities in receiving an extracorporeal membrane oxygenation (ECMO) therapy at type A hospitals which have their own services and resources in performing ECMO. Critical COVID-19 patients can receive ECMO therapy if they meet ECMO indications after the patient has received therapy in the porn position and maximal ARDS ventilator therapy according to the clinician. ECMO indications are PaO2/FiO2 <50 mmHg for >3 hours or PaO2/FiO2 <60 mmHg for >6 hours (2).

The inhibited interaction between the system of circulation and foreign body happens uninterruptedly in the ECMO circuit for patients receiving ECMO support, during an extracorporeal life support (ECLS) leading a normal hemostatic condition to shift to a hypercoagulable state, resulting in the patient being at risk for thrombosis. In addition, several complications can also accompany the ECMO support, namely bleeding, embolism, and heparin-induced thrombocytopenia (HIT). HIT is an illness condition identified with the

prevalence of thrombocytopenia and a higher threat of thrombosis (3). This report presented a case of ECMO support in critically ill COVID-19 patient at Soetomo Hospital in Surabaya, Indonesia.

## CASE PRESENTATION

A referral female patient with confirmed Pneumonia COVID-19, 27years old, came to Soetomo Hospital from PHC hospital on December 3rd 2020 with P1001 post C-section. The patient complained for cough and out of breath from 10 days before the admission. She also had fever from 3 days before the admission. No history of asthma, diabetes mellitus and hypertension were found. Later, COVID-19 diagnosis was then confirmed with the mixed type of respiratory failure, obesity grade 3, and hypernatremia. Her laboratory examination results showed elevation of white blood cells (WBC) 38.270/$m^3$, neutrophil – lymphocyte ratio (NLR) 26,6, interleukin-6 791,10 pg/mL, d-dimer level 2.940 ng/mL; liver function: aspartate aminotransferase (AST) 35 U/L, alanine aminotransaminase (ALT) 61 U/L; renal function: blood urea nitrogen (BUN) 22 mmol/L, creatinine serum 0,6 mmol/L; inflammatory reaction markers: procalcitonin (PCT) 0,01ng/ml, C-reactive protein (CRP) 0,1 mg/L; and blood gas analysis: pH: 7,217, pO2: 62, pCO2: 85,7, HCO3: 34,9, BE: 7, SaO2: 91%, FiO2: 100%, P/F ratio 62. After admission, she was planned for ECMO support.

### Treatment

On the 1st day, patient was treated immediately with mechanic ventilation and sedated with dexmedetomidine 0,4 mcg/kg/hour, midazolam 3 mg/hour and rocuronium 50 mg/hour. She was also therapeuticized with heparin 10.000 unit/24 hours due to the elevation of d-dimer level. Meanwhile, as for protocol therapy to treat her COVID-19, she received remdesivir at 100 mg/24 hours as antiviral, dexamethasone at 6 mg/24 hours, n-acetyl cysteine at 600 mg/8 hours, vitamin C injection at 1 gram/24 hours, vitamin D at 5000 UI/24 hours and zinc at 50 mg/24 hours. After intubation on 2nd day, the saturation of patient's blood oxygen was still uneasy to be maintained with the index of oxygenation at 90% and blood gas analysis exhibited pH: 7,384; pO2: 62, pCO2: 63,6; HCO3: 37,9; BE: 13; FiO2: 85% and PF ratio: 72. Based on that, on the 2nd day, VV-ECMO treatment was performed and placed in the left femoral and right jugular vein to rescue her (figure 1 and 2).

Figure 1

Figure 2

During extracorporeal life support (ECLS), patient got a deep sedation treatment, and also at the same time, anticoagulant heparin sodium was given with dose of 35.000 UI/24 hours and pumped continuously. Then, the dose of heparin was increased by 40.000 unit/24 hours on the 3rd day, 45.000 unit/24 hours on 5th day, and 50.00 unit/24 hours on the 6th day. Later, the dose of heparin was tapered down until 30.000 unit/24 hours on the 8th day.

The problems appeared during ECMO, which were the leakage at cannulation, intra oral and tracheal bleeding, and hematuria.

On the 9th day after ECMO support, patient was planned for decannulation, based on her parameter oxygenation (SaO2 97%; FiO2 60%) and blood gas analysis.

## DISCUSSION

The manifestation of COVID-19 symptoms can be mild and cured. Most of the patients need no medicine to cure. However, some patients may experience a worsening condition, thus, they are able to fall into a severe and critical level that requires intensive treatment. Indeed, some patients can experience ARDS which can progress to multiple organ failures and even death (4). A standard COVID-19 treatment consists of prone positioning, sedation, lung recruitment, protective lung ventilation strategy, neuromuscular blockade, optimal positive end-expiratory pressure, and volume optimalization (5).

COVID-19 patients with ARDS require other oxygen therapy because their mechanical ventilation is no longer able to provide optimal oxygen support. The role of ECMO is very important in this regard. Thus, the application of ECMO for severe and critical COVID-19 patients is growing rapidly. At the beginning of the pandemic, the use of ECMO was very limited, while the ECMO installation guidelines were based on best practice at that time (6). However, the preference in using ECMO support should be considered individually derived by the assessment of its risks and benefits provided for the patients by realizing the presence of some unavoidable contraindications (5).

This case report presented the first successful case of using ECMO for severe and critical COVID-19 patients at Soetomo Hospital in Surabaya. The patient was a referral patient from PHC hospital with worsening condition, therefore on the second day after admission, the patient was planned to undergo an ECMO therapy. The patient was a post-C-section woman with grade 3 obesity. The patient had received antibiotic and antiviral therapy as well as mechanical ventilation, but her oxygenation support was still difficult to maintain.

Prior to initiating the ECMO cannulation, the baseline laboratory values should be obtained consisting of a complete blood component, activated clotting time d-dimer (ACT), prothrombin time/international normalized ratio (INR), antithrombin activity (AT), fibrinogen, and thromboelastography (TEG). In addition, at 10 minutes prior to cannulation, heparin was administered to the patient at a dose of 50 U/kg. The dosage of heparin intravenous infusion can be raised to 2-20 U/kg/hour with the condition of ACT value is <180 seconds targeting at ACT level within 180-200 seconds along with the activated partial thromboplastin time (aPTT) within 50-80 seconds (5). Most typically, the application of heparin in ECMO is because its easiness to be found, rapid onset of action, and its capability to convert its action with protamine. However, some inherent limitations are found in heparin due to its tendency in persisting any fluctuations in the sensitivity of dosages and heparin-induced thrombocytopenia (HIT) (7).

During ECMO support, the patient received anticoagulant therapy to avoid clotting as the implication of any direct interaction between blood circulation and the ECMO circuit. The patient was initially treated with a heparin pump at 30,000 units/24 hours on the first day of ECMO support. Then it was gradually increased at 50,000 units/24 hours. As a result, during ECMO support, the patient experienced bleeding in the form of leakage in the cannulation, intraoral and tracheal bleeding, and hematuria. The cause of bleeding occurrence in the patient during ECMO support may be associated to the incidence of acquired von Willebrand syndrome (AVWS), enhanced-fibrinolytic-type DIC, the counter implications of utilizing the endothelitis associated anticoagulant therapy and vascular fragility. If any indication appeared that the bleeding cause is AVWS, then the most appropriate strategy in stopping the bleeding is to discontinue the application earlier. A reduction in anticoagulant dose should be considered, is any anticoagulant therapy is indicated to be too strong, even though the risk of thrombosis is definitely increased. Any enforcement from the bleeding cause is very fundamental in COVID-19 patients who utilize ECMO support (8).

For patients with COVID-19, both antifibrinolytic therapy and anticoagulant therapy with heparin should be performed at the same time in the provision of ECMO support in which fibrinolytic-type DIC displays an expansion as a complication. Especially, the application of heparin together with the anti-thrombin group is expected to prove effective (9).

Otherwise, if there is any significant thrombosis in the oxygenator, along with the growth in d-dimer levels at >10 g/mL, fibrinogen at <1.5 g/L, and a decline in the number of platelets, the whole ECMO circuit pack which includes both oxygenator and tubing should be substituted despite the satisfactory gas exchange function. If any significant bleeding or the need for invasive procedures occurs, the reduction or suspension of heparin was performed for a short period for declining ACT below 150 seconds, and blood transfusions can be performed if necessary (5).

In this patient, bleeding occurred as an adverse effect from the use of anticoagulants. Thus, in overcoming this problem, gradual reduction of heparin dose was performed until the decannulations of ECMO.

During the application of ECMO, there are several parameters needing to be monitored. The first parameter is ACT value as a point of care test (POCT) of the whole blood in which the mix between blood and an activator is performed to produce the whole hemostasis functional examination. Second, the parameter of anti-factor XA activity levels (Anti-XA) serves as the accurate implication of unfractionated heparin concentration in supplying the adequate anticoagulation. Activated partial thromboplastin time (aPTT) as parameter should also be monitored as an examination based on plasma which is utilized as an activator, calcium, and phospholipids in calculating the duration for fibrin formulation in the cellular components' absence. Furthermore, thromboelastography (TEG) is also a parameter which must be surveilled during ECMO support. It is a method of testing the efficiency of blood coagulation from examining the viscoelastic properties in formatting clots to calculate the durability of the coagulation cascade from the moment of fibrin formation to clot lysis with the inclusion of platelets plays major role significantly (10).

This case is the first case with ECMO patient to survive. Despite all the problems faced during ECMO support, she can survive until she was declared cured of COVID-19 infection. Changes in coagulation conditions in COVID-19 patients greatly affect ECMO support, so anticoagulant therapy during ECMO support is very important.

## CONCLUSION

A rise of coagulation in patients with COVID-19 was exhibited by the altering value of coagulation parameters. The anticoagulants treatment using ECMO support is very fundamental in patients with COVID-19 particularly related to treatment dosage and administration. Monitoring the clinical conditions and laboratory tests are needed to determine the dose of anticoagulation.

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