Supplementary Online Content

Mustafa AK, Alexander PJ, Joshi DJ, et al. Extracorporeal membrane oxygenation for patients with COVID-19 in severe respiratory failure. *JAMA Surg*. Published online August 11, 2020. doi:10.1001/jamasurg.2020.3950

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Text

DATA COLLECTION, POPULATION, AND SETTINGS

Data was collected retrospectively from 40 consecutive patients with COVID-19 in severe respiratory failure supported with ECMO. COVID-19 infection was confirmed using PCR-based assays. All patients were treated at Advocate Christ Medical Center and Rush University Medical Center from March 17th, 2020, onwards. 75% were transferred from outside hospitals. ECMO procedures were performed from March 22nd to April 27th. Follow-up data was obtained until July 17th.

The research protocol was approved by the institutional review boards at both Advocate Christ Medical Center and Rush University Medical Center (IRB No. AHC-7426-C5000376 and ORA-20040401, respectively). Waiver of the need for consent was obtained. The data was de-identified during analysis and publication to protect patient privacy. These data and patients have not been previously reported.

The following data was collected: demographics, laboratory values, hemodynamics, mechanical ventilator and ECMO settings, medications administered, radiographic imaging such as chest x-rays, microbiology results including COVID-19 tests, any complications incurred including renal failure as defined by the need for renal replacement therapy, patient disposition and other pertinent information.

Race/ethnicity information was obtained from hospital records. This information was collected in order to identify any characteristic that might demonstrate vulnerability to COVID-19 infection.

PATIENT SELECTION

The following were absolute contraindications to ECMO placement: patients with cardiac arrest without return of spontaneous circulation; lactate ≥ 14 mMol/L or pH ≤ 6.9; those in multi-system organ failure; those with known life expectancy < 5 years prior to SARS-CoV-2 infection; those with known devastating neurological injury; patients with recent hemorrhagic stroke or any known major bleeding diathesis; patients with known Do Not Resuscitate/Do Not Intubate (DNR/DNI) status; those who refuse to receive blood transfusions; those with permanent immobility; cases of known active malignancy; and finally, patients with severe, symptomatic chronic organ failure, such as cirrhosis, end-stage renal disease on dialysis, end-stage cardiomyopathy or those with severe chronic lung disease requiring home oxygen therapy.

The following criteria were used to determine if a patient would be an ECMO candidate: patients ≤ 70 years old, and who were suffering from severe hypoxia or hypercapnia despite maximum ventilator support similar to what was described by the EOLIA trial group[1] – i.e. if arterial blood gas (ABG) deteriorates to the point where the partial pressure of oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) ratio (P/F ratio) is < 50 for more than 3 hours, < 80 for more than 6 hours, or if pH < 7.25, partial pressure of carbon dioxide ($PaCO_2$) > 60 mm Hg for more than 6 hours. Maximized ventilator settings constituted a minimal FiO_2 of > 0.8, positive end expiratory pressure (PEEP) > 10 cm H_2O, and tidal volumes of 6 mL/kg predicted body weight, while keeping a plateau pressure < 32 cm H_2O.

OUTCOME MEASURES

The primary outcome was survival following safe discontinuation of mechanical ventilation and ECMO support. The time spent in various phases of treatment such as mechanical ventilation and ECMO were also determined. Trends in laboratory data, and the types and frequencies of complications, including mortality, were determined.

STATISTICAL ANALYSIS

Data are expressed as mean ± standard error of the mean, median and range as appropriate.

QUALITY CONTROL

The data analysis was reviewed by multiple authors to ensure accuracy.

CANNULATION TECHNIQUE AND TREATMENT PROTOCOL

The very first ECMO was performed with dual internal jugular (IJ)/femoral vein cannulas (21/27 Fr, respectively). Despite optimal positioning and flows, the patient developed severe hypoxemia prompting urgent cannula exchange with a single access, dual-stage right atrium-to-pulmonary artery cannula. Due to the successful result, we adopted this technique for all subsequent ECMOs.

In the operating room, a trans-esophageal echocardiogram was performed to evaluate cardiac function. Veno-venous ECMO was initiated using a 29 or 31 Fr Protek-Duo TandemHeart cannula (CardiacAssist Inc., Pittsburgh, PA). Percutaneous access through the right IJ vein was obtained with ultrasound guidance. The Seldinger technique was then used for cannulation with the tip of the cannula positioned in the main pulmonary artery distal to the pulmonic valve under fluoroscopic and echocardiographic guidance **(eFigure 1)**. This cannula provided flows of up to 4.5 L/min, sufficient for ECMO purposes, with direct blood return into the main pulmonary artery and beyond the pulmonic valve. The advantages of this particular cannulation strategy are detailed in the discussion section. 5,000 units of IV heparin was given just prior to ECMO initiation. ECMO flows were typically maintained between 3-4.5 L/min with line pressure in the ECMO circuit kept under 300 mm Hg.

Patients were then brought to the Cardiac Surgery ICU, and immediately started on anticoagulation with a direct thrombin inhibitor for a PTT goal of 45-70 seconds. Once off ECMO, patients were transitioned to warfarin, with an INR goal of 2.5-3.5, or Eliquis, depending on institutional preference.

Inhaled pulmonary vasodilator therapy was instituted. Vasopressors were weaned as tolerated while maintaining SBP above 90 mm Hg. Oral quetiapine was started and all other sedatives such as propofol, midazolam, fentanyl, dexmedetomidine etc., were weaned in order to expedite extubation. Mild analgesics such as acetaminophen or tramadol were used as needed. In consultation with Infectious Diseases specialists, hydroxychloroquine, antivirals, antibiotics, and IL-6 inhibitors were administered. Patients were treated with steroids until discharge in order to combat the overwhelming cytokine response to the infection. Diuretics were also employed in all patients.

Early nasogastric tube feeding was initiated to optimize nutrition.

Weaning of mechanical ventilator support was accomplished by weaning PEEP and FiO_2 while maintaining adequate oxygenation and normal lactic acid levels. Respiratory rate and tidal volume were also decreased as tolerated.

Laboratory data and chest radiographic trends were monitored. When deemed safe, pressure support trials were initiated, and patients were extubated. They were then mobilized with help from our expert nursing staff, as well as respiratory and physical therapists.

Swallow evaluation was undertaken to transition to oral feeding.

ECMO FiO_2 and sweep flows were also weaned while maintaining adequate oxygenation and normal lactic acid levels. The oxygenator was then disconnected, and patient observed for 24 hours to ensure adequate oxygenation and ventilation before removal of the ECMO cannula. This was performed at the bedside, and the cannulation site closed with a purse-string suture.

Inhaled pulmonary vasodilators were weaned off along with quetiapine and diuretics as tolerated.

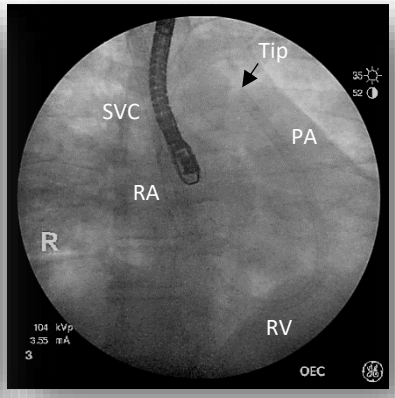
Patients were transferred from the Cardiac Surgery ICU to a non-ICU COVID unit from where they were discharged home (or to a rehabilitation center if needed).

eReference.

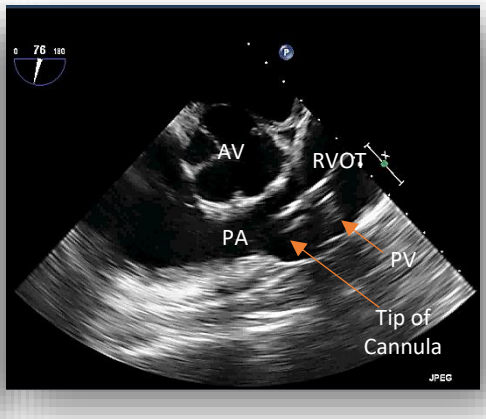
1. Combes A, Hajage D, Capellier G, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. *N Engl J Med*. 2018;378(21):1965–1975.

eFIGURE. ECMO Technique

Cannula Insertion



Fluoroscopy



Trans-Esophageal Echocardiography

Single cannula inserted in the right neck region through the internal jugular vein. Tip of cannula resting in the main pulmonary artery and beyond the pulmonic valve indicated by an arrow in the fluoroscopy and echocardiography images. Abbreviations: AV – Aortic Valve, PA – Pulmonary Artery, PV – pulmonic valve, RA – Right Atrium, RV – Right Ventricle, RVOT – Right Ventricular Outflow Tract, SVC – Superior Vena Cava.