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Case report

Outcomes of extracorporeal membrane oxygenation in adult patients with hypoxemic respiratory failure refractory to mechanical ventilation

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ABSTRACT

Introduction: Extracorporeal membrane oxygenation (ECMO) is a mode of extracorporeal life support that has been used to support cardiopulmonary disease refractory to conventional therapy. The experience with the use of ECMO in acute hypoxemic respiratory failure is still limited. The aim of this study was to report clinical outcomes in adult patients with acute hypoxemic respiratory failure refractory to mechanical ventilation treated with ECMO.

Methods: Between July 2011 and October 2017, 18 adult patients with hypoxemic respiratory failure refractory to mechanical ventilation were admitted to the Intensive Care Unit of an acute care tertiary hospital in Barcelona, Spain. These patients were treated with ECMO as salvage respiratory therapy. Outcomes included clinical data, ventilatory and blood gas characteristics, survival, and complications.

Results: Fifteen patients (83.3%) were previously treated in prone position. The indication of VV-ECMO was established at an early stage after a mean (SD) of 3.8 (2.5) days on mechanical ventilation. The mean duration of ECMO was 10.4 days, and 16 patients (88.9%) required venous cannulation, mostly femoral-internal jugular. The mean length of ICU stay was 27 days and the mean hospital stay was 42.1 days. The ICU survival rate was 55.5% (n = 10) and the hospital survival rate was 50% (n = 9).

Conclusions: This clinical study in a small series of ICU patients treated with ECMO confirms the usefulness of this technique as a ventilatory support in patients with refractory hypoxemic respiratory failure. However, the indication of this procedure is also committed to an ethical reflection considering the possible futility of the measure on a case-by-case basis and associated complications.

1. Introduction

The severe forms of acute respiratory distress syndrome (ARDS) have a very high mortality over 45% as defined at the Berlin consensus Conference [1] and remain a challenge for the clinician. The occurrence of severe rapid-onset ARDS causing refractory hypoxemia during the 2009 influenza A (H1N1) pandemic, prompted resurgence of extracorporeal life support techniques, including extracorporeal membrane oxygenation (ECMO). It has been shown that early use of ECMO in combination with protective ventilation gives favorable results in severe hypoxemia [2–5] and should be included in the treatment algorithm of ARDS [2]. The use of veno-venous ECMO (vv-ECMO) in patients with ARDS and refractory hypoxemia and/or hypercapnia promotes lung recovery by allowing ultraprotective ventilation strategies and resting the lungs [3], which may be associated with an increase in survival. The installation of ECMO reduces the risk of lung injury caused by mechanical ventilation and minimizes intraalveolar pressure in positive pressure mechanical ventilation, promoting ultraprotective ventilation [6,7] using plateau airway pressure < 25 cm H_2O, tidal volume < 3 mL/kg, high positive-end expiratory pressure (PEEP) > 8–10 cm H_2O, with respiratory frequency of ≤10 per minute, and a fraction of inspired oxygen (FiO_2) of < 0.6 [2,3].

The predictable reversibility of lung lesions and the absence of any other therapeutic limitation are indispensable prerequisites to the use of ECMO [2]. vv-ECMO has evolved substantially and has become a widespread technique with progressively improving outcomes in recent years [8]. Appropriate patient selection, timing and use of validated treatment options, including prone positioning before initiation of

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extracorporeal support have been reported to be key factors for treatment success [9]. Systematic reviews and meta-analysis have provided encouraging results in patients with refractory ARDS who receive veno-venous ECMO with survival rates around 60% at hospital discharge despite initial high illness severity [9,10]. However, real-life studies are needed to further assess the optimal use, outcomes, and different aspects of ECMO care. The aim of this study was to report clinical outcomes in adult patients with acute hypoxemic respiratory failure refractory to mechanical ventilation treated with ECMO.

2. Materials and methods

2.1. Study design

Between July 2011 and October 2017, a case series study was performed at the ICU of a single acute-care tertiary hospital (Hospital Universitario de Bellvitge) in Barcelona, Spain, in which 34 acute-care beds and 4 intermediate-care beds are available. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and the protocol was approved by the Institutional Review Board. Since the patients in this study were all sedated and ventilated, written informed consent was obtained from the patient's next of kin.

2.2. Patients

Critically ill adult patients with ARDS and hypoxemia refractory to lung-recruitment maneuvers and prono positioning were eligible for veno-venous ECMO. Extracorporeal life support was considered if despite a protective ventilation strategy (involving the use of prone positioning) the PaO_2/FiO_2 ratio was below 50 mm Hg when $FiO_2 = 1$ for at least 3 hours, if the PaO_2/FiO_2 ratio was below 80 mm Hg when $FiO_2 = 1$ for more than 6 hours, and/or if there was respiratory acidosis with pH < 7.20 for over 6 hours. Patients with massive pulmonary embolism and acute right ventricular dysfunction (acute cor pulmonale) were also candidates for ECMO. Veno arterial ECMO must be considered in cardiogenic shock, and vv-ECMO in ARDS with isolated respiratory failure. But there is a special situation in acute cor pulmonale which could have indication of vv-ECMO. In severe forms of ARDS, patients often have evidence of acute right heart failure and pulmonary arterial hypertension because hypoxemia, hypercarbia and acidosis are very potent pulmonary vasoconstrictors. In vv-ECMO therapy the pulmonary perfusión with oxygenated blood leads to a fall in the right heart afterload improving right ventricular cardiac output.

Exclusion criteria were as follows [11]: contraindications to anticoagulation, including active bleeding or high risk of bleeding; intracranial bleeding or potentially hemorrhagic intracranial lesions; duration of mechanical ventilation ≥ 7 days; severe immunosuppression; multiorgan failure syndrome (Sequential Organ Failure Assessment [SOFA] score > 15); coma following cardiac arrest; unpredictable reversibility of lung lesions; age > 70 years; body mass index (BMI) > 35 kg/m^2; and moribund patients with a very low chance of meaningful survival with ECMO treatment.

2.3. Study procedures and data collection

Patients underwent ultrasound-guided vascular cannulation following expert panel recommendations [2], with femoral-jugular venous access using a 23–29 F cannula for drainage and 19–21 F for return, and confirmation of correct position of the cannulas. A non-occlusive centrifugal pump system (CARDIOHELP HLS set Advanced, Maquet/Getinge Group Spain, S.L., Madrid, Spain) and the Rotaflow RF-32 Centrifugal Pump, with cannulas of sufficient diameter to allow flow rates of 4–7 L/min were used. The oxygenator membrane is made from polymethylpentene. Percutaneous femoral and internal vein cannulation was performed in the ICU by the cardiac surgery team with the medical support of intensivists. The extracorporeal system and the venous cannulas were also removed in the ICU.

Data recorded in all patients included demographics (age, sex), anthropometric parameters, SOFA score, comorbid diseases, respiratory and ventilation characteristics, hemodynamic and vasoactive features, complete biochemical profile with lactate, complete hemogram and coagulation tests, transfusion requirements, complications related and unrelated to ECMO, and status at ICU discharge.

Descriptive statistics are presented. Categorical variables are expressed as frequencies and percentages, and continuous variables as mean and standard deviation (SD).

3. Results

During the study period, a total of 18 patients, 11 men and 7 women, with a mean (SD) age of 44.0 (12.6) years and a mean BMI of 29.1 (3.5) kg/m^2 underwent ECMO. The mean SOFA score was 10 (4.0). Eleven patients (61.1%) had a potentially reversible pulmonary cause (bacterial/viral/fungal infections) bacterial or viral (H1N1 virus) in septic patients secondary to pneumonia in 7, invasive pulmonary aspergillosis in 2, *Pneumocystis jirovecii* pneumonia in 1, smoke inhalation injury in 1. Causes of ARDS in the remaining 7 (38.9%) patients included respiratory distress in the immediate postoperative period after cardiac surgery in 3, immunosuppression in 2 septic patients diagnosed with B-cell and T-cell lymphoma, respectively, acute pancreatitis with septic shock in 1, and thrombotic thrombocytopenic purpura in 1 (Fig. 1). All patients had received corticosteroids and 15 (83.3%) patients required vasopressor support. Severity-related data and respiratory parameters before the introduction of ECMO are shown in Table 1. Prone positioning before ECMO was used in 15 patients (83.3%) and nitric oxide to improve acute pulmonary hypertension in 7.

Veno-venous ECMO was performed in 16 (88.9%) patients and veno-arterial ECMO in the remaining 2. The mean duration of ECMO was 10.4 days. The mean flow at 24 hours after ECMO initiation was 4.4 (0.8) L/min and at terminating ECMO 4.1 (0.7) L/min.

Pneumothorax occurred in 6 patients and acute renal failure in 7 patients, 5 of which required real replacement procedures. Transfusion of blood derivatives was necessary in 14 patients and 15 (83.3%) patients required vasopressor support. Complications related to the ECMO procedure are shown in Table 2. Bleeding was the most frequent complication (72.2%) followed by hypovolemia (66.7%), and thrombocytopenia (50%).

The mean duration of mechanical ventilation was 25.5 (16.7) days. Percutaneous tracheostomy for minimizing airway lesions due to prolonged orotracheal intubation and to facilitate weaning was performed

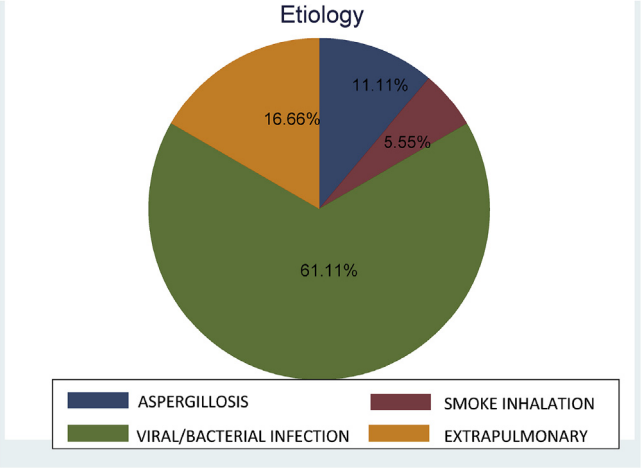

Fig. 1. ARDS etiology in VV ECMO patients.