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CASE REPORT

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Extracorporeal CO_2 removal and renal replacement therapy in acute severe respiratory failure in COVID-19 pneumonia: Case report

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Abstract

The COVID-19 pandemic significates an enormous number of patients with pneumonia that get complicated with severe acute respiratory distress syndrome (ARDS), some of them with refractory hypercapnia and hypoxemia that need mechanical ventilation (MV). Those patients who are not candidate to extracorporeal membrane oxygenation (ECMO), the extracorporeal removal of CO_2 ($ECCO_2R$) can allow ultra protective MV to limit the transpulmonary pressures and avoid ventilatory induced lung injury (VILI).

We report a first case of prolonged $ECCO_2R$ support in 38 year male with severe COVID-19 pneumonia refractory to conventional support. He was admitted tachypneic and oxygen saturation 71% without supplementary oxygen. The patient's clinical condition worsens with severe respiratory failure, increasing the oxygen requirement and initiating MV in the prone position. After 21 days of protective MV, $PaCO_2$ rise to 96.8 mmHg, making it necessary to connect to an $ECCO_2R$ system coupled continuous veno-venous hemodialysis (CVVHD). However, due to the lack of availability of equipment in the context of the pandemic, a pediatric gas exchange membrane adapted to CVVHD allowed to maintain the removal of CO_2 until completing 27 days, being finally disconnected from the system without complications and with a satisfactory evolution.

1 | INTRODUCTION

Protective mechanical ventilation (MV) involves the use of low tidal volumes (Vt) in order to reduce transpulmonary pressure levels to avoid damage induced by MV. That clinical practice has demonstrated to improve survival in patients with respiratory distress syndrome (ARDS).[1,2] However, an undesirable consequence of protective MV is hypoventilation and hypercapnia,[3] acute pulmonary hypertension, diminished myocardial contractility, reduced renal blood flow, and release of endogenous catecholamins.[4] Hypercapnic acidosis associates to increase hospital mortality, prolonged hospital stay, and a reduction in survival with $PaCO_2$ greater than 65 mmHg.[5] Molecular studies had shown a close association between hypercapnia and alveolar cell membrane repair disorders, alveolar clearance, and local immune response.[6]

Gattinoni 1986 designed the first device that separated the ventilatory support from oxygen supply, which made possible to optimize lung protection during VM.[7] That was the first published $ECCO_2R$ system, which allowed the removal of CO_2 from the blood through a gas exchange membrane, without oxygenating the blood in a meaningful way.[2]

TABLE 1 Clinical parameters

Parameters		$ECCO_2R$				
Laboratory	Basal	24 h	7 days	14 days	27 days	24 h post $ECCO_2R$
Hemoglobin (gr/L)	119	75	81	76	68	8,2
Leukocytes (10^9/L)	8.8	13.7	15.2	14.2	16.3	13870
Platelets (10^9/L)	398	321	176	166	393	408000
CRP (nmol/L)	722.8	761.9	1160	1583	393.3	310.4
Ureic nitrogen (mmol/L)	5.0	5.7	7.0	6.4	21.5	55
Creatinine (umol/L)	53.0	23.5	23.5	35.36	79.5	0.97
Sodium (mmol/L)	133.0	136.4	134.0	141.0	143.0	141
Potassium (mmol/L)	4.3	4.8	4.7	3.7	4.6	4.8
Ventilatories						
Vt (ml/kg ideal)	3.0	2.5	2.5	3.0	4.0	4.0
RR (breaths/min)	60	24	26	24	30	30
PEEP (cmH_2O)	4	4	4	4	4	4
Plateau pressure (cmH_2O)	18	18	19	19	18	18
Distension pressure (cmH_2O)	13	14	15	15	14	14
Compliance (ml/cmH_2O)	16	16	15	15	16	16
PaO_2/FiO_2	81.4	157.4	178.2	207.1	233.0	234.2
Blood gases						
pH	7.21	7.37	7.37	7.40	7.40	7.39
PaO_2 (mmHg)	94.4	78,7	77.0	93.2	94.3	82.0
$PaCO_2$ (mmHg)	96.8	54.4	50.7	49.4	42.0	45.0
Bicarbonate (mmol/L)	37.5	30.9	29.2	30.2	25.7	26.7
Lactate (mmol/L)	0.7	0.6	0.7	-	-	-
$ECCO_2R$						
Blood flow (ml/min)	500	400	300	320	400	-
Oxygen flow (L/min)	7	7	7	6	4	-
CO_2 removal (ml/min)	-	-	61	57	-	-
Hemodynamics						
Mean arterial pressure (mmHg)	89	77	78	124	74	91
HR (heartbeat/min)	88	106	119	83	101	98
Norepinephrine dose (ug/kg/min)	0.01	0.10	0.00	0.00	0.00	0.00

Abbreviations: CRP, C-reactive protein; $ECCO_2R$, extracorporeal CO_2 removal; FiO_2, inspired oxygen fraction; HR, heart rate; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure; RR, respiratory rate; TV: tidal volume.

In the 1990 s, *Young et al*. was the first to report a system that coupled $ECCO_2R$ to continuous renal replacement therapy (CRRT) through an arterio-venous low flow CO_2 removal device.[8–10] In 2013, Forster and colleagues showed a similar device that combined CVVHD associated a $ECCO_2R$ using blood flow less than 500 ml/min in patients with severe ARDS.[11]

We present the first case of a patient with severe respiratory failure due to COVID-19 pneumonia in whom CO_2 removal therapy is performed using a pediatric oxygenation membrane coupled to HDVVC.

2 | CASE PRESENTATION

A 38-year-old male with a history of overweight, hypothyroidism and insulin resistance begin with progressive dyspnea and presented to

the emergency department for evaluation. Upon admission he was in poor general conditions, febrile, tachypnea, oxygen saturation 71% without supplementary oxygen, blood pressure 108/80 mmHg, heart rate 111 beats/min. Laboratory exams (Table 1) showed paO_2 73 mmHg, pCO_2 35 mmHg, bicarbonate 22 mmol/L, hemoglobin 120 g/L and creatinine 74,2 umol/L. Respiratory indirect immunofluorescence results negative, a positive polymerase chain reaction for COVID-19 and thorax computed tomography (CT) was suggestive of COVID-19 pneumonia (Figure 1). The patient was transferred to the intensive care unit (ICU).

Ventilatory support was initiated with high-flow nasal cannula, prone position ventilation, antibiotics, steroids (1 mg/kg) for 5 days and anticoagulation with low molecular weight heparin for suspected pulmonary thromboembolism. The seventh day in the ICU, he evolves with high oxygen requirements starting invasive MV, analgesia and deep sedation, neuromuscular blockade, and prone position for 10 consecutive days. The 15th day of MV he presented a left pneumothorax that required pleural drainage with adequate lung re-expansion; however, this event cause a progressive deterioration of the gas exchange. In the following days it was difficult to maintain the protective MV and then he developed severe hypercapnic respiratory insufficiency. After 21 days in MV, it was decided to connect the patient to an $ECCO_2R$ system with Braun OMNI® machine through a 23 cm, 14.5 French (Fr) hemodialysis catheter to remove CO_2. The CO_2 removal membrane was installed pre-hemodialysis filter to achieve greater efficiency, as described by Terragni.[12] After the initiation of therapy, a progressive reduction of $PaCO_2$ levels observed, which allowed to an ultra protective MV (Table 1). During the entire period of the $ECCO_2R$ therapy, it was ensured appropriate systemic anticoagulation with non-fraction heparin with a target activated partial thromboplastin time (aPTT) of 70–80 seconds.

During the first days of therapy, the patient remained in the original $ECCO_2R$ OMNI® Braun system requiring change of the oxygenator membrane and the dialysis filter every 72 h, as suggested by the manufacturer. However, the patient needed prolonged $ECCO_2R$ support unfortunately, due to a shortage circuit supply, it was necessary to create an adapted circuit with a pediatric membrane oxygenator

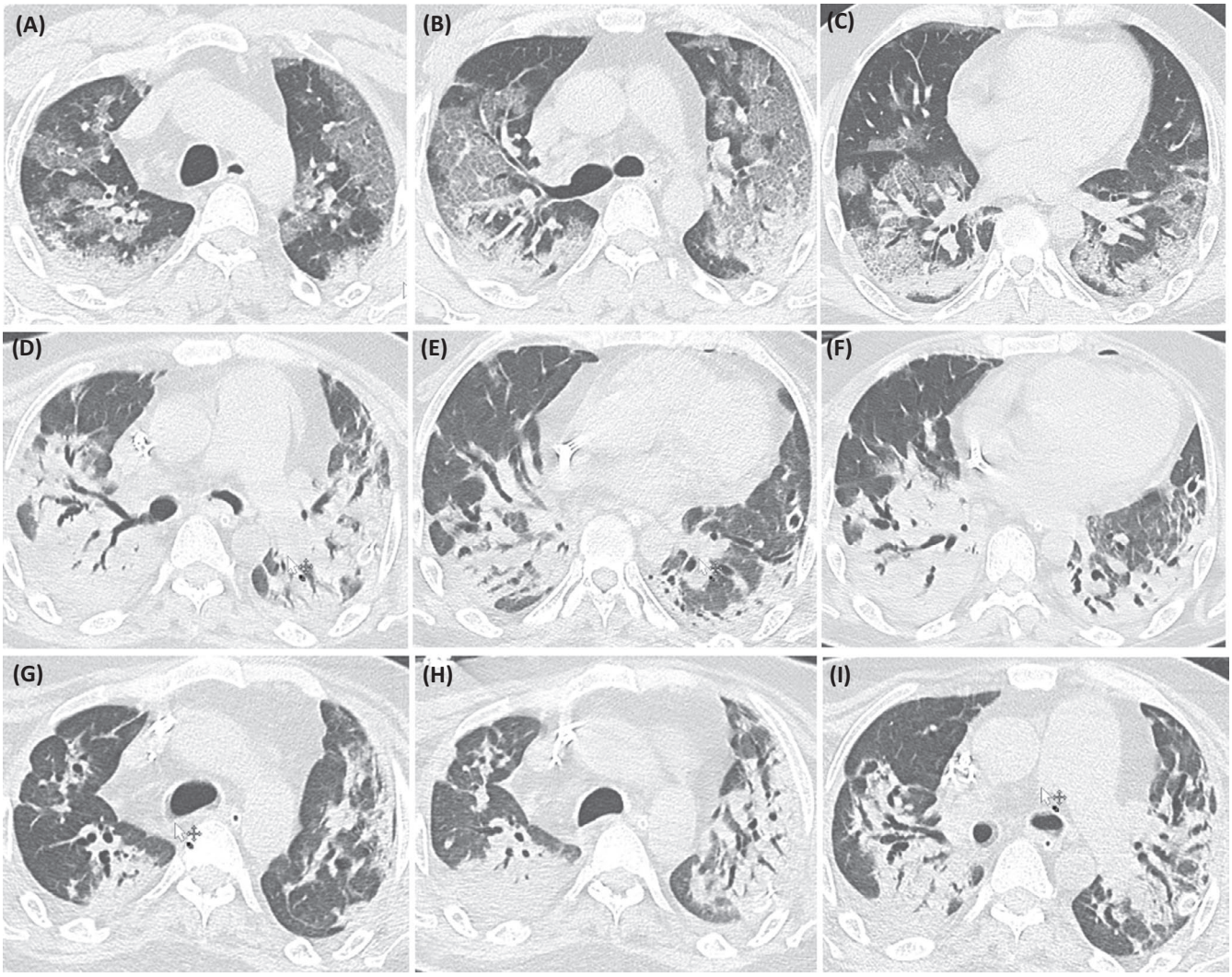

FIGURE 1 Computed tomography (CT) of the chest during evolution: A, B, C: basal; D, E, F: 10 days of $ECCO_2R$ and G, H, I: 48 h of retirement of $ECCO_2R$

connected to a DIAPACT® Braun machine (Figure 2). This new circuit was kept under optimal anticoagulation and the system operated efficiently for 17 consecutive days, without evidence of pediatric membrane oxygenator failure. After 27 days of $ECCO_2R$ support, the system was disconnected. During the entire period of $ECCO_2R$ support there was no evidence of hemorrhagic, hematological, or infectious complications (Figure 3).

The patient continued his evolution in a stable way, he was able to disconnect from the MV without complications and he was discharged from the hospital to his home.

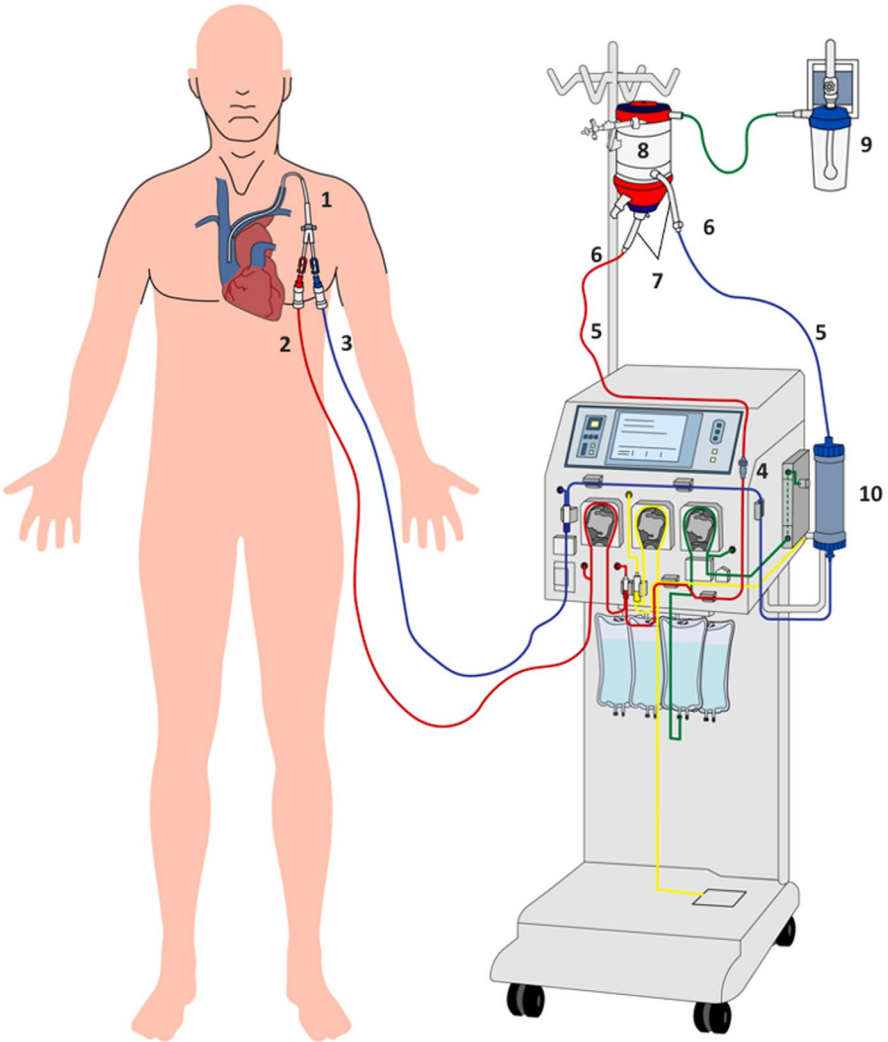

FIGURE 2 Adapted oxygenation membrane system for removal of CO_2: Red line: pre CO_2 removal, blue line: post CO_2 removal, 1: hemodialysis catheter, 2: arterial lines, 3: venous line, 4: male / male DIN connector, 5: ⅜ to ¼ connector , 6: line ⅜, 7: CO2 exchange membrane, 8: oxygen network, 9: line ⅛, 10: dialyzer [Colour figure can be viewed at wileyonlinelibrary.com]

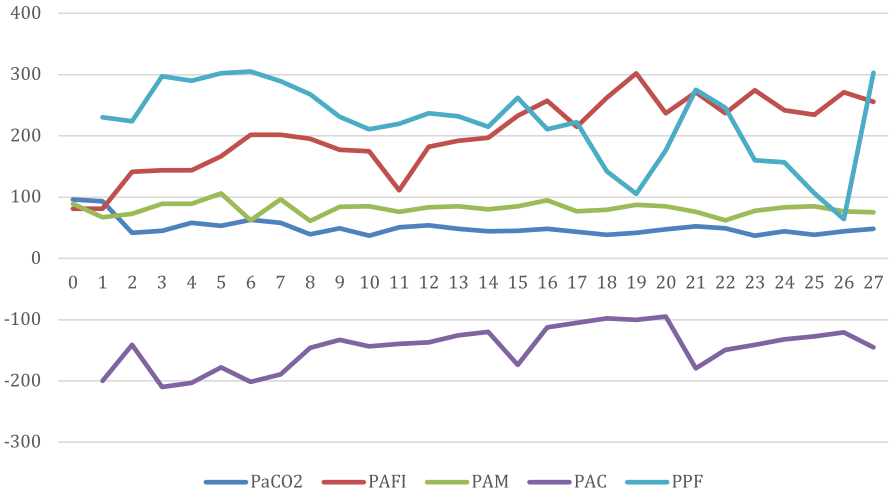

FIGURE 3 Ventilatory and hemodynamic parameters. The days of treatment with $ECCO_2R$ are plotted on the horizontal axis. $PaCO_2$: partial pressure of carbon dioxide, PAFI: PaO_2 / FiO_2, PAM: mean arterial pressure, PAC: circuit arterial pressure, PPF: pre filter pressure [Colour figure can be viewed at wileyonlinelibrary.com]

3 | DISCUSSION

CO_2 extracorporeal removal systems, both the extracorporeal membrane oxygenation (ECMO) and $ECCO_2R$, are useful in multiple clinical scenarios, but in ARDS the $ECCO_2R$ should be considered in cases of pH<7.25, $PaCO_2$ >65 mmHg, and PaO_2/FiO_2 >80.[4] The decision of $ECCO_2R$ coupled with CVVHD depends on the need renal support and the availability of trained nursing staff.

The $ECCO_2R$ are partial low-flow respiratory support systems that can be implemented with membranes of different surfaces (0.33 to 1.81 m^2) and allows extraction of 25% of the CO_2 content in the blood, reducing ventilatory requirements.[4,13] The CO_2 diffusion capacity is 20 times greater than oxygen, which allows the system to purify CO_2 at low flows of blood (Qb <500 ml/min). The main determinant of CO_2 diffusive capacity is the blood flow and less important is the flow of oxygen, with a maximum efficacy at 6–8 L/min.

Different publications have demonstrated the utility of $ECCO_2R$ systems in severe ARDS.[14] Among them, the SUPERNOVA study confirmed the benefits of $ECCO_2R$ in this group of patients, minimizing the respiratory acidosis and achieving ultra protective MV with the use of membranes of 0.59 to 1.3 m^2 and blood flow between 200 to 1,000 ml/min.[15]

The clinical use of $ECCO_2R$ systems has been described not only in ARDS but also in chronic obstructive pulmonary disease patients, weaning from MV and as a bridge therapy in lung transplant.[16] The $ECCO_2R$ allows to reduce the ventilatory demand, decrease Vt to 3–4 ml/kg of ideal weight and to keep plateau pressures less than 25 cmH_2O and driving pressures of less than 15 cmH_2O allowing ultra protective MV in a safe way, with less risk of hemorrhagic complications related to the vascular access, lower costs, less technical difficulties with less need of trained staff. ECMO system is a more complex technique, requires greater blood flows and bigger vascular cannulas (21 to 31 Fr).[4]

As we noted before, the success of the $ECCO_2R$ systems depends on vascular access that can achieve blood flow rate up to 500 ml/min and of anticoagulation to maintain aPTT ranges between 70 and 80 seconds.[17–19] The latter is crucial to maintain membrane patency and avoid membrane fouling. In our clinical case, we had two episodes of circuit clotting despite optimal anticoagulation. The possible explanations of this that there are blood-membrane interaction, activation of the coagulation cascade and a slowdown of the blood in the oxygenator membrane.

The patient in our clinical case had a formal contraindication of ECMO because the respiratory failure and consequent respiratory acidosis ($PaCO_2$ 96.8 mmHg and pH 7.21) presented at day 21 of MV, and that was the reason we choose for an $ECCO_2R$ strategy as a rescue supportive therapy.[20]

The use of devices for CO_2 removal as a support strategy in selected critical patients is not new in our environment and has been used for more than a decade. A great number of $ECCO_2R$ system currently available requires specialized technology and machines specifically designed for this purpose, which can make this technology less accessible. What is distinctive about the present case is that it was the first patient who was treated with CO_2 removal for several weeks, the use of the pediatric oxygenation membrane coupled to HDVVC made it possible to efficiently treat respiratory failure and CO_2 retention, maintaining ultra-protective MV using low Vt for a long period of time.

In this case of severe respiratory failure by COVID-19, the innovation of the therapy was able to stabilize gas exchange of the patient and lung function until recovery and withdrawal of invasive MV.

4 | CONCLUSION

This report presents a clinical case of severe hypercapnic respiratory acidosis in which the use of an oxygenation membrane coupled to CRRT allowed after 27 days to reduce the lung injury associated with MV, stabilizing the patient's gas exchange at a low cost.

$ECCO_2R$ associated with HDVVC is a safe and effective therapy in reducing CO_2, correcting respiratory acidosis and allowing ultra-protective MV.

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CONFLICT OF INTERESTS

The authors have no financial conflicts of interest to declare.

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