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Case Report

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Case Report: When Enough is not Enough…Treating Refractory Hypoxemia

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ABSTRACT

Herein we report a case of a 43 year old immunocompromised male, post renal transplant, with Adult Respiratory Distress Syndrome (ARDS), secondary to Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), who required Veno-Venous Extra Corporeal Membrane Oxygenation (VV ECMO), with the unique configuration of double oxygenators.

Despite invasive ventilatory support and maximum conventional VV ECMO support, he had persistent refractory hypoxemia. At this point, it was deemed necessary to attempt an adjuvant intervention to improve his oxygenation and hence the decision was made, to add another oxygenator to the existing ECMO circuit. His oxygenation parameters improved after the addition of the second oxygenator. The patient improved gradually and we continued to wean his ECMO settings. He was eventually DE cannulated after 34 days on ECMO.

We believe that this is the first case where two oxygenators were placed in parallel, in a single circuit, for a SARS COV-2 patient with refractory hypoxemia. The addition of an oxygenator in parallel was successful in improving oxygenation and more importantly allowed us to continue with ultra-protective lung ventilation.

The patient provided informed consent for scientific publication.

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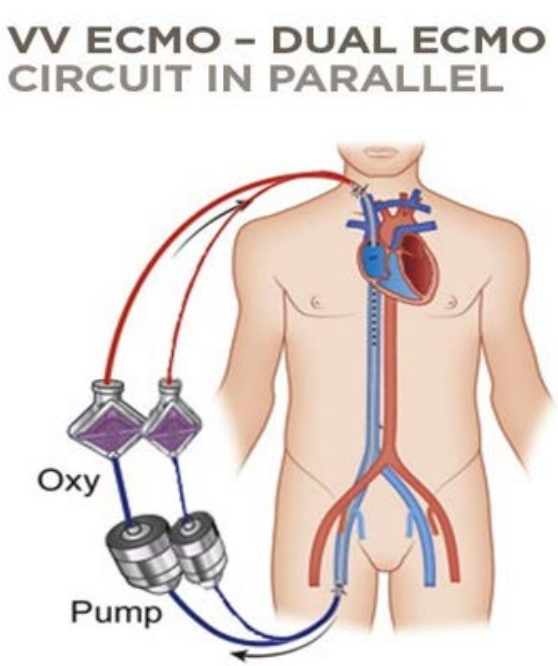
Case Description

A 43 year old male patient was admitted to our hospital from another facility, with SARS COV-2 pneumonia, for possible ECMO. History included renal transplant 10 years previously. He presented with recent evidence of chronic rejection (report from transplant hospital), despite being on immune-suppression with tacrolimus, mycophenolate and prednisolone. SARS COV-2 was confirmed with Rt-PCR. Chest X-ray (CXR) initially showed moderate patchy infiltrates bilaterally, and he was treatment included, dexamethasone 6mg once daily and one dose of Sotrovimab 500mg iv (given within 5 days of symptom onset). His immunosuppression therapy was withheld. Although he stabilized for a short period of time on high flow nasal cannula, his condition deteriorated with progressive hypoxemia and he required higher oxygen support. We opted to first use NIV (Non-invasive ventilation), and then to initiate VV ECMO while on NIV, with an aim to avoid intubation. A 25 Fr drainage cannula was inserted in the right femoral vein and a 19 Fr return cannula in the right internal jugular vein. He was maintained on "awake ECMO" for a short period of time but unfortunately, his clinical

condition continued to deteriorate. CXR showed complete "white out," signifying severely consolidated lungs. Since he had a very high respiratory drive that was compromising ECMO flow, he was intubated. This, despite sweep being set at 10 L/min. At this stage, he also required renal replacement therapy as his urine output had diminished significantly.

Despite being ventilated, deeply sedated, on a NMB (neuro-muscular blocker) and VV ECMO, the patient remained hypoxemic with low PO2 and saturations less < 80%. ECMO was flowing maximally at 5L/min, set at 100 % oxygen and a sweep of 10L/min. At this point, it was deemed necessary to attempt an adjuvant intervention to improve his oxygenation and hence the decision to add another oxygenator to the existing ECMO circuit (Figure 1). Two oxygenators were run in parallel on a single circuit with a Y connector placed in the drainage tubing approximately 20cm from the cannula in the R femoral vein and the circuit was split into two tubes each going to an oxygenator. Two Maquet Cardio-help machines were used simultaneously. A tube from each oxygenator would then converge to the Y connector attached to the receiving cannula also about 20cm before the cannula in the R internal jugular vein. The oxygenator capacity was 5L/ min and 7L/ min flow respectively.



Characteristics	Before ECMO	ECMO (Single)		ECMO (Double)	
				ECMO 1	ECMO 2
ECMO settings					
Blood flow rate, L/min	NA	5		2	3
Sweep gas flow rate, L/min		10		3.5	3.5
Fraction of delivered oxygen		1.0		1.0	1.0
Arterial blood gas results		**Before Intubation**	**After Intubation**		
pH	7.36	7.39	7.39	7.47	
Partial pressure of arterial carbon dioxide, mm Hg	36.6	36.9	36.7	30.3	
Partial pressure of arterial oxygen, mm Hg	51.4	47	52	67.1	
Lactates, mmol/L	0.9	1.5	0.8	1.1	
Oxygen saturation, %	88	78	88	95	
P/F ratio, PaO_2/FIO_2					
Mechanical ventilator settings					
Mode	High flow nasal cannula	Non invasive ventilation	PRVC	PRVC	
Fraction of Inspired Oxygen	0.9	1.0	0.8	0.4	
Flow, L/min	60				
Respiratory rate, breaths per minute		26	12	8	
Tidal volume, mL		200	120	100	
Positive end expiratory pressure, cm H_2O		7	10	8	
P/F ratio, PaO_2/FIO_2	57.11	47	52	67.1	

Figure 1: Double VV ECMO circuit with double oxygenator in parallel with two Y connector in a single circuit

Total ECMO flow remained the same as the flow that had been flowing through the single oxygenator at 5L/min. This flow was split with 2L flowing through the smaller oxygenator and 3L flowing through the larger oxygenator respectively. The FiO2 was set at 1 and sweep flow at 5L/min for both oxygenators.

Despite satisfactory oxygen parameters, the patient continued to have a high respiratory drive even with the sweep settings mentioned, when stopping the NMB, hence *partial paralysis* and sedation was used to achieve the desired spontaneous breathing rate. Oxygen parameters improved after the procedure. Gradually we continued to wean his ECMO settings, but as he would still be requiring prolonged ventilation, a percutaneous tracheostomy was performed. This was complicated by non-surgical bleeding from the tracheostomy site into his airway, which required aggressive management with blood products and repeated bronchoscopic interventions. In view of ongoing bleeding, consumptive coagulopathy and the need for multiple transfusions, a decision to change the circuit back to a single oxygenator was made (Day 27). Changing the circuit resulted in a significant reduction in bleeding, and over the next 2-3 days, he was eventually DE cannulated after being on ECMO for 34 days. After extensive rehabilitation, he was discharged home after 87 days.

Discussion

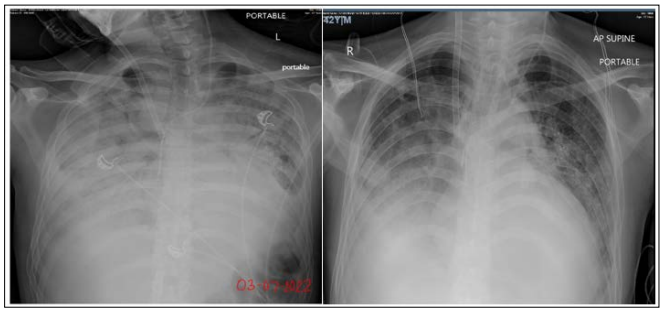
Despite being on conventional VV ECMO, our patient had persistent refractory hypoxemia. Although lactate was normal, we predicted that this patient would not survive additional complications in view of his refractory hypoxemia. Although proning was an option, this was considered high risk as the patient developed significant instability even with the slightest assisted movement. An option that we considered, was to increase flow by adding another drainage catheter in the left femoral vein. Since the flow at this present oxygenator's maximum capacity, approximately 5L/min, and since there was an increased chance of recirculation phenomenon, we decided against this option. We also discussed using another separate circuit inserted in the left internal jugular for return and the left femoral to drain, as described by Patel et al [1]. We were concerned about issues with the two cannulas in the neck and also using up all venous access points. Rather, it was thought prudent to use the existing circuit, right -sided cannulations, to add another oxygenator with a larger flow capacity of 7L/min in parallel sequence.

Recent mortality data in patients with SARS-COV-2, who require ECMO, as reported by ELSO, was nearly 50% despite applying conventional adjunctive measures possible [2]. This prompted our effort to improve the patient's oxygenation by adding a second oxygenator. In patients with refractory hypoxemia, single ECMO

circuits may fail to provide the oxygen delivery necessary to meet the physiological demand [3]. The success of a second circuit to improve oxygenation has been previously reported, but data are limited to small case series [4, 5].

We believe that this is the first case where two oxygenators were placed in parallel in a single circuit for SARS COV-2 patient with refractory hypoxemia. The addition of an oxygenator in parallel was successful in improving oxygenation and more importantly allowed us to continue with ultra -protective lung ventilation. Furthermore, when a complication did occur in the form of sepsis, the patient was able to maintain tissue perfusion despite an increase in oxygenation requirement. Although total flow was the same as through a single oxygenator, oxygen delivery through two circuits increased, as was reflected in improved saturations and PO2 (table 1). Although this configuration does not address the problem of decreased ECMO flow to cardiac output it does address the core issue of oxygenation directly [6].

We therefore propose that using our simple single circuit, dual oxygenator configuration is as effective as any other augmented circuit configuration and may be effectively used to treat refractory hypoxemia in any instance of severe ARDS.



Before intubation & Double ECMO initiation CXR before weaning Double ECMO
(Day 13 ICU stay) (Day 38 ICU stay)

Chest X Rays of Patient during ICU Stay

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