Elevated oxygen demand in a case of COVID-19 with severe ARDS: a point for optimal oxygenation therapy including ECMO management

Taku Oshima (✉ t_oshima@chiba-u.jp)

Chiba University Graduate School of Medicine <https://orcid.org/0000-0002-3868-8272>

Takehiko Oami

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Mana Yamashiro

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Akiko Higashi

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Yosuke Hayashi

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Natsumi Suga

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Shin Takayanagi

Department of Infectious Diseases, Chiba University Hospital

Seiichiro Sakao

Department of Respiriology, Chiba University Graduate School of Medicine

Taka-aki Nakada

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine

Case report

Keywords: Coronavirus disease 2019 (COVID-19), SARS-CoV-2, acute respiratory distress syndrome (ARDS), VV-ECMO, indirect calorimetry, oxygen consumption (VO₂)

Posted Date: August 6th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-51286/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has become a global pandemic, and those developing critically ill conditions have been reported to have mortality in the range of 39% to 61%. Due to the lack of definitive treatments, mechanical ventilation and supportive oxygenation therapy are key management strategies for the survival of patients with acute respiratory distress syndrome (ARDS). Optimizing oxygenation therapy is mandatory to treat patients with severe respiratory failure, to sufficiently compensate for the oxygen (O_2) demand. We experienced a case of severe ARDS due to COVID-19 successfully treated with extracorporeal membrane oxygenation (ECMO) after increasing oxygen delivery according to O_2 consumption measurement by indirect calorimetry

Case Presentation: A 29-year-old obese but otherwise healthy man was hospitalized for treatment of COVID-19 pneumonia presenting with a 4-day history of persisting cough, high fever, and dyspnea. Mechanical ventilation, nitric oxide inhalation, and prone positioning were initiated in the ICU against severe respiratory dysfunction. Indirect calorimetry on the 3rd and 6th ICU days revealed persistent elevation of oxygen consumption (VO_2) of 380 mL/min. Veno-venous ECMO was initiated on the 7th ICU day after further deterioration of respiratory failure. Periodic events of SpO_2 decline due to effortful breathing was not resolved by neuromuscular blockade in attempt to reduce O_2 consumption. Increasing the ECMO flow induced hemolysis and hyperkalemia despite the use of large bore cannulas and ECMO circuit free of clots and defects. The hemoglobin management level was elevated from 10 g/dL to 13 g/dL to increase blood oxygen capacity, enabling the reduction of ECMO flow while attenuating respiratory effort and maintaining SpO_2 . Lung protective ventilation strategy and prone positioning were continued for successful weaning from ECMO on the 16th ICU day, and the ventilator on the 18th ICU day.

Conclusion: The present case of severe ARDS due to COVID-19 was successfully treated with ECMO. Enhancing oxygen delivery was crucial to compensate for the elevated O_2 demand. Measuring O_2 consumption by indirect calorimetry can elucidate the oxygen demand for optimizing the oxygenation therapy for successful management and survival of critically ill COVID-19 patients.

Background

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has become a global pandemic (1-3), and those developing critically ill conditions have been reported to have mortality in the range of 39% to 61% (4-6). Due to the lack of definitive treatments prove effective for COVID-19, mechanical ventilation and supportive oxygenation therapy are key management strategies for the survival of patients with acute respiratory distress syndrome (ARDS) (7).

The goal of oxygenation therapy for ARDS is to provide sufficient oxygen (O_2) to meet the demand of the whole-body metabolism. Hypoxia can occur when oxygen delivery insufficiently compensates for the O_2 demand, either as a result of reduced oxygen uptake or the excessive elevation of oxygen consumption.

COVID-19 is suggested to induce severe systemic inflammation (8, 9), possibly leading to hypermetabolism and elevated O₂ consumption.

For progressive respiratory failure despite optimal conventional management such as prone positioning and nitric oxide (NO) administration, extracorporeal membrane oxygenation (ECMO) support is indicated (10, 11). Moreover, measures to increase the efficacy of O₂ supplementation become critical when O₂ demand exceeds delivery, and reduction of O₂ consumption is not feasible. However, methods to determine O₂ demand of COVID-19 patients have not been well described to date.

Here, we encountered a case of severe ARDS due to COVID-19 successfully treated with ECMO by optimizing oxygen delivery against persistent elevation of O₂ demand revealed by indirect calorimetry.

Case Presentation

A 29-year old male admitted to a clinic after 4 days of persisting cough, high fever, and dyspnea, without gastrointestinal symptoms or loss of taste and smell. He was obese with body mass index (BMI) of 31.9 kg/m² (height 168 cm, weight 90.0 kg), but otherwise presented no underlying pathologies, did not travel abroad and worked at home for at least 14 days prior to the onset of the symptoms. He was diagnosed positive for SARS-CoV-2 polymerase chain reaction test the day after his admission and referred to our hospital for treatment of COVID-19 pneumonia. His brother, a nursing home employee, living in the same household was later diagnosed SARS-CoV-2 positive.

He was conscious and communicated verbally upon admission but presented high fever and tachypnea of 30/minute, with persisting cough requiring 6 L/min of O₂ to maintain SpO₂ 95%. Blood tests revealed non-bacterial inflammatory signs, with white blood cell count of 5,900/mm³ with slightly reduced lymphocyte count of 985/mm³, CRP 5.29 mg/dL, procalcitonin 0.14 ng/mL, and interleukin-6 86.8 pg/mL [Table 1]. He also presented bilateral ground-glass opacities and patchy consolidation on the lung computed tomography (CT) scan, typical findings of COVID-19 pneumonia [Figure 1a, 2a]. Favipiravir and azithromycin were started on the day of hospitalization, but SpO₂ fell below 92% under 15L/min O₂ reservoir mask on day 3, when he was intubated and admitted to the intensive care unit (ICU).

Mechanical ventilation was initiated, and nitric oxide was inhaled at 20 ppm for oxygenation support. Chest X ray on the 3rd ICU day presented severe progression of bilateral infiltrate, prompting prone positioning for lung recruitment. Indirect calorimetry [E-COVX, General Electric, USA] was conducted on the 3rd ICU day for the evaluation of energy and O₂ consumption [Table 2]. The resting energy expenditure (REE) ranged from 1832 to 2583 kcal/day, corresponding to O₂ consumption volume (VO₂) of 275 and 380 ml/min, respectively, while being deeply sedated with midazolam and fentanyl to achieve -5 points on the Richmond agitation-sedation scale (RASS). Repeated evaluation on the 6th ICU day revealed sustained REE of 2530 kcal/day with VO₂ of 380 ml/min.

His lung oxygenation gradually deteriorated and required positive end-expiratory pressure (PEEP) 14 cm H₂O for PaO₂/FiO₂ of 85 on the 6th ICU day, leading to the decision to start veno-venous (VV) ECMO [centrifugal pump: RotaFlow®, Maquet Getinge, Rastatt, Germany; artificial lung: BIOCUBE 6000®, NIPRO, Osaka, Japan; drainage and outflow catheter: 25Fr.HLS cannula®, 19Fr.HLS cannula®, Maquet Getinge, Rastatt, Germany] on the 7th ICU day [Figure 2b]. ECMO was initiated at blood flow of 4 L/min, with 7L/min of 100% O₂ as sweep gas, with blood temperature managed at 37.0°C. NO was paused and ventilatory support was minimized [bi-level pressure control ventilation with FiO₂ 0.4 at PEEP 10cm H₂O and driving pressure 5 cm H₂O] as lung protective strategy, while prone positioning was continued.

Events of excessive respiratory effort were observed after the initiation of VV-ECMO, with a simultaneous SpO₂ decline below 80%. As the patient was already deeply sedated with midazolam and fentanyl to achieve Richmond agitation-sedation scale of -5, neuromuscular blocking with rocuronium was added to attenuate the excessive respiratory effort, thus to avoid lung damage and to reduce O₂ consumption. However, unresolved SpO₂ decline with gradual increase of lactate from 1.2 to 1.8mmol/l under stable systemic circulation necessitated increasing the ECMO blood flow to 4.5 L/min. However, the increased flow induced hemolysis and hyperkalemia, without obvious signs of sucking down or clot formation in the ECMO circuit and artificial lung. We strategically elevated the hemoglobin management level from 10 g/dL to 13 g/dL to enhance the blood oxygen capacity and thus the O₂ delivery, enabling the reduction of the ECMO blood flow to resolve hemolysis.

Chest X-ray findings presented gradual recovery from bilateral infiltration, enabling reduction of ECMO flow to 2.6L/min for sufficient oxygenation by the 12th ICU day. He was weaned off from ECMO on the 16th ICU day after 120 minutes of a successful sweep gas cessation trial. He was successfully weaned off from the ventilator on 18th ICU day and was transferred back to the ward on the 23rd ICU day. After 23 days of rehabilitation in the ward, he was discharged home on his 46th day of hospitalization [Figure 1b, 2c].

Discussion And Conclusions

We experienced a case of young COVID-19 patient suffering from severe ARDS. Oxygen delivery by VV-ECMO was optimized to compensate for the increased O₂ demand as observed in indirect calorimetry, for successful management and survival.

While young COVID-19 patients rarely develop critically ill conditions, (5, 12) obesity (BMI≥30 kg/m²) has been observed in 46% of the critically ill COVID-19 patients (5). The current case had BMI of 31.9 kg/m² and presented bilateral ground-glass opacities and patchy consolidation on the CT scan, typical of acute respiratory distress syndrome in COVID-19 with reduced lung compliance (13). Although VV-ECMO is indicated, mortality for COVID-19 patients with severe respiratory failure has been reported to be as high as 50% (7). Appropriate management of ECMO is essential for the safety and efficacy of the treatment, thus survival of the patients (11).

While oxygenation failure can only be evaluated passively by the amount of O₂ supplementation required to maintain adequate blood oxygen levels, O₂ consumption can be measured by indirect calorimetry, a method to measure VO₂ and carbon dioxide production (VCO₂) by respiratory gas analysis to calculate energy expenditure (14). Oxygen demand in critically ill COVID-19 patients has not been well described, with only one study reporting a median REE of 4044 kcal/day in seven critically ill patients without ECMO, corresponding to VO₂ of 585 mL/min (18), more than twice the average (270mL/min) reported in critically ill patients (15). The elevated demand for oxygen is likely to be sustained during the course of respiratory failure, leading to the need for VV-ECMO and additional measures to increase the efficacy of O₂ delivery (17, 19). As indirect calorimetry is not readily available for patients under ECMO (19, 20), it is recommended to conduct calorimetry soon after initiation of mechanical ventilation to optimize O₂ delivery according to the O₂ demand.

Indirect calorimetry was conducted in the present case on the 3rd and 6th ICU days, before the initiation of VV-ECMO. VO₂ reached 380ml/min while being deeply sedated at RASS -5. The REE of 2583kcal/d corresponds to 1.6 times the energy requirements calculated by the Harris-Benedict equation using ideal body weight (1563kcal/d), comparable to stress factor for calculating energy demands in 50 % total body surface area burns. The elevated VO₂ persisted until the 6th ICU day, reflecting the sustained O₂ demand. Increasing O₂ delivery with VV-ECMO was required to maintain systemic oxygenation, under normal temperature management with ECMO and efforts to reduce O₂ consumption by administering sedatives and neuromuscular blockers to achieve RASS -5. Since increasing the ECMO flow induced hemolysis despite the use of large bore catheters (25Fr for drainage and 19Fr for outflow) and no obvious signs of suck down or clot formation in the circuit and the artificial lung, blood hemoglobin level was elevated to increase the blood oxygen capacity and thus the O₂ delivery (17).

In conclusion, we experienced a COVID-19 patient with severe ARDS, successfully managed by VV-ECMO. While VV-ECMO was an effective salvage treatment for respiratory failure despite vigorous mechanical ventilation, measures to enhance oxygen delivery was crucial to compensate for the elevated O₂ demand. Measuring O₂ consumption by indirect calorimetry can elucidate the oxygen demand for optimizing the oxygenation therapy for successful management and survival of critically ill COVID-19 patients.

List Of Abbreviations

COVID-19, Coronavirus disease 2019; ARDS, acute respiratory distress syndrome; O₂ oxygen; NO, nitric oxide; ECMO, extracorporeal membrane oxygenation; BMI, body mass index; CT, computed tomography; ICU, intensive care unit; REE, resting energy expenditure; VO₂, O₂ consumption volume; PEEP, positive end-expiratory pressure; VV, veno-venous; VCO₂, carbon dioxide production.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: We have obtained consent for publication from the patient's family.

Availability of data and materials: The patient data obtained from a medical record are available through the corresponding author upon a reasonable request.

Competing interests: The authors declare no conflict of interests related to the current case report.

Funding: None

Authors' contributions:

Acquisition of data: YH

Drafting of the manuscript: MY, AH, NT, TO

Critical revision of the manuscript for important intellectual content: NT, TO, TO, TN

Supervision: TN

All authors have read and approved the final manuscript.

Acknowledgements: Not applicable

References

1. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *Jama*. 2020;323(16):1574–81.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020;382(18):1708–20.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *Jama*. 2020;323(20):2052–9.
4. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med*. 2020;382(21):2012–22.
5. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet*. 2020;395(10239):1763–70.
6. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8(5):475–81.

7. Li X, Guo Z, Li B, Zhang X, Tian R, Wu W, et al. Extracorporeal Membrane Oxygenation for Coronavirus Disease 2019 in Shanghai, China. *Asaio j.* 2020;66(5):475–81.
8. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, et al. Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure. *Cell Host Microbe.* 2020;27(6):992–1000.e3.
9. Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol.* 2020;20(6):363–74.
10. Komindr A, Abe R, Tateishi Y, Takahashi Y, Goto J, Wada K, et al. Establishing extracorporeal membrane oxygenation team increased number of patients and improved data recording. *J Intensive Care.* 2019;7:11.
11. Kowalewski M, Fina D, Słomka A, Raffa GM, Martucci G, Lo Coco V, et al. COVID-19 and ECMO: the interplay between coagulation and inflammation-a narrative review. *Crit Care.* 2020;24(1):205.
12. Argenziano MG, Bruce SL, Slater CL, Tiao JR, Baldwin MR, Barr RG, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. *Bmj.* 2020;369:m1996.
13. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Crit Care.* 2020;24(1):154.
14. Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger CP, Hiesmayr M, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. *Clin Nutr.* 2016. doi:10.1016/j.clnu.2016.06.010. [Epub ahead of print].
15. Oshima T, Ragusa M, Graf S, Dupertuis YM, Heidegger CP, Pichard C. Methods to validate the accuracy of an indirect calorimeter in the in-vitro setting. *Clinical nutrition ESPEN.* 2017;22:71–5.
16. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2019;38(1):48–79.
17. Spinelli E, Bartlett RH. Relationship between hemoglobin concentration and extracorporeal blood flow as determinants of oxygen delivery during venovenous extracorporeal membrane oxygenation: a mathematical model. *Asaio j.* 2014;60(6):688–93.
18. Yu PJ, Cassiere H, DeRosa S, Bocchieri K, Yar S, Hartman A. Hypermetabolism and COVID-19. *JPEN J Parenter Enteral Nutr.* 2020.
19. Cheypesh A, Yu X, Li J. Measurement of systemic oxygen consumption in patients during extracorporeal membrane oxygenation—description of a new method and the first clinical observations. *Perfusion.* 2014;29(1):57–62.
20. De Waele E, van Zwam K, Mattens S, Staessens K, Diltoer M, Honore PM, et al. Measuring resting energy expenditure during extracorporeal membrane oxygenation: preliminary clinical experience with a proposed theoretical model. *Acta Anaesthesiol Scand.* 2015;59(10):1296–302.

Tables

Table 1. Laboratory data on ICU admission day

Hematology			Biochemistry		
WBC	11400	/mm ³	AST	79	IU/L
RBC	430×10 ⁴	/mm ³	ALT	78	IU/L
Hemoglobin	13.0	g/dL	LDH	545	IU/L
Hematocrit	38.1	%	ALP	218	U/L
Platelet	19.3×10 ⁴	/mm ³	TP	5.8	g/dL
<hr/>			Albumin	2.7	g/dL
			UN	8	mg/dL
			Creatinin	0.74	mg/dL
			T-Bil	0.6	mg/dL
			D-Bil	0.2	mg/dL
			Amylase	190	IU/L
			CPK	643	IU/L
			CRP	16.9	mg/dL
			Glucose	106	mg/dL
			Sodium	131	mEq/L
<hr/>			Potassium	4.2	mEq/L
PT	11.2	sec	Chloride	100	mEq/L
PT%	87	%	Calcium	7.4	mg/dL
PT-INR	1.02		<hr/>		
APTT	34.0	sec			
FDP	2.8	µg/mL			
Fibrinogen	479	mg/dL			
Others					
Interleukin-6	164.3	pg/mL			
Procalcitonin	0.46	ng/mL			
Ferritin	1225	ng/mL			
<hr/>					
Blood gas analysis					
pH	7.39		Blood	Negative	
PaO ₂	58	mmHg	Sputum	Negative	
PaCO ₂	39	mmHg	<hr/>		
HCO ₃ ³⁻	23.6	mmol/L			
BE	-1.2	mmol/L			
Lactate	0.9	mmol/L			
			Urinary antigen test		
			<i>Streptococcus pneumoniae</i>	Negative	
			<i>Legionella</i>	Negative	

WBC: white blood cell, RBC: red blood cell, PT: prothrombin time, INR: international normalized ratio, APTT: activated partial thromboplastin time, FDP: fibrin degradation products, BE: base excess, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, TP: total protein, UN: urea nitrogen, T-Bil: total bilirubin, D-Bil: direct bilirubin, CPK: creatine phosphokinase, CRP: C-reactive protein

Table 2. Results of indirect calorimetry and vital signs during the measurement.

ICU day	Duration (min)	3						6	
		15	30	45	60	75	90	15	30
REE	(kcal/day)	1879	1842	1903	1946	2049	2583	2530	2548
RQ		0.65	0.70	0.72	0.68	0.64	0.70	0.62	0.64
VO ₂	(mL/min)	280	271	279	288	306	380	380	380
VCO ₂	(mL/min)	182	190	201	196	196	266	235	243
Heart rate	(bpm)	63	61	63	63	68	74	68	68
SpO ₂	(%)	95	95	95	99	85	77	94	94
Body temperature	(°C)	38.5	38.5	38.5	38.5	38.6	38.6	38.0	38.2
Respiratory rate	(/min)	25	24	25	23	40	48	24	25
Minute volume	(L/min)	8.4	8.2	8.9	7.8		14.0	10.2	10.4
RASS					-5			-4	

REE: resting energy expenditure; RQ: respiratory quotient; VO₂: volume of oxygen consumption, VCO₂: volume of carbon dioxide production; SpO₂: oxygen saturation; RASS: Richmond Agitation-Sedation Scale

Figures

a) 1st Hospital Day

b) 45th Hospital day

Figure 1

Lung CT Scan on admission and before discharge. a) Bilateral ground glass opacities and patchy consolidations typical of COVID-19 pneumonia was observed on admission. b) The initial findings have

resolved with slight remains of ground glass appearance by the day before discharge.

a) 1st Hospital day

b) 9th Hospital (7th ICU) day

c) 43rd Hospital day

Figure 2

Chest x-ray progression during the hospital stay. a) Minor shadows observed in the lower lobes on hospital admission. b) Severe bilateral infiltration progressed with the deterioration of respiratory function, requiring VV- ECMO. c) Although slight bilateral shadows remain, respiratory function sufficiently recovered, no longer requiring oxygen supplementation at the time of hospital discharge.