Supplemental Online Content

Kurihara C, Manerikar A, Querrey M, et al. Clinical characteristics and outcomes of patients with COVID-19–associated acute respiratory distress syndrome who underwent lung transplant at an academic medical center in the US. *JAMA*. doi:10.1001/jama.2022.0204

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

eMethods

Lung transplantation

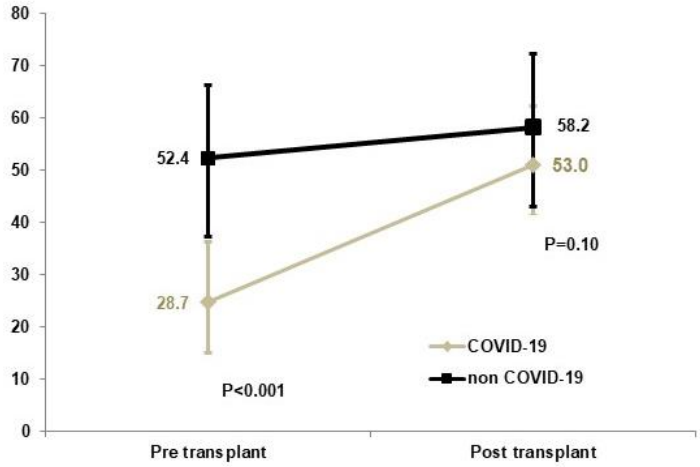
All patients with COVID-19 received treatment according to the institutional standard of care from a multidisciplinary care team that included surgeons, infectious disease physicians, pulmonary and critical care physicians, and cardiologists. Each COVID-19 patient was treated by the multidisciplinary care team over the entire duration of the illness before being considered for transplantation. Referral for lung transplantation was made when there was no longitudinal evidence of lung recovery as agreed by the multidisciplinary team. Lung transplant evaluation was performed according to the International Society for Heart and Lung Transplantation guidelines [1, 2]. The broad transplant criteria for patients with CCAA included: Age ≤70 years old; negative SARS-CoV-2 PCR by two consecutive lower respiratory fluid, either tracheal aspirate of bronchoalveolar lavage, collected 24 hours apart; single organ failure; no evidence of irrecoverable brain damage [3], and body mass index ≤35, which was similar to the non-COVID-19 patients. Those being considered for multiorgan transplantation were excluded for the purposes of this study. Donation after cardiac death or ex vivo lung perfusion (EVLP) were not utilized.

Details of the transplant management for patients in this series are provided in a prior report [3]. Briefly, COVID-19 ARDS patients underwent double lung transplant using an approach of central veno-arterial ECMO. All patients received the same immunosuppression and post-operative management. Induction immunosuppression included methylprednisolone 500mg and basiliximab 20mg intraoperatively. Additionally, a second dose of basiliximab was administered on post-operative day 4. The maintenance immunosuppression included prednisone (0.5mg/kg daily), mycophenolate mofetil (1000mg twice a day) and tacrolimus (0.015mg/kg total daily to target drug levels between 8-12 ng/ml). All patients received standard protocol driven infection prophylaxis after lung transplantation. Following the acute hospitalization, the patients were considered for inpatient rehabilitation.

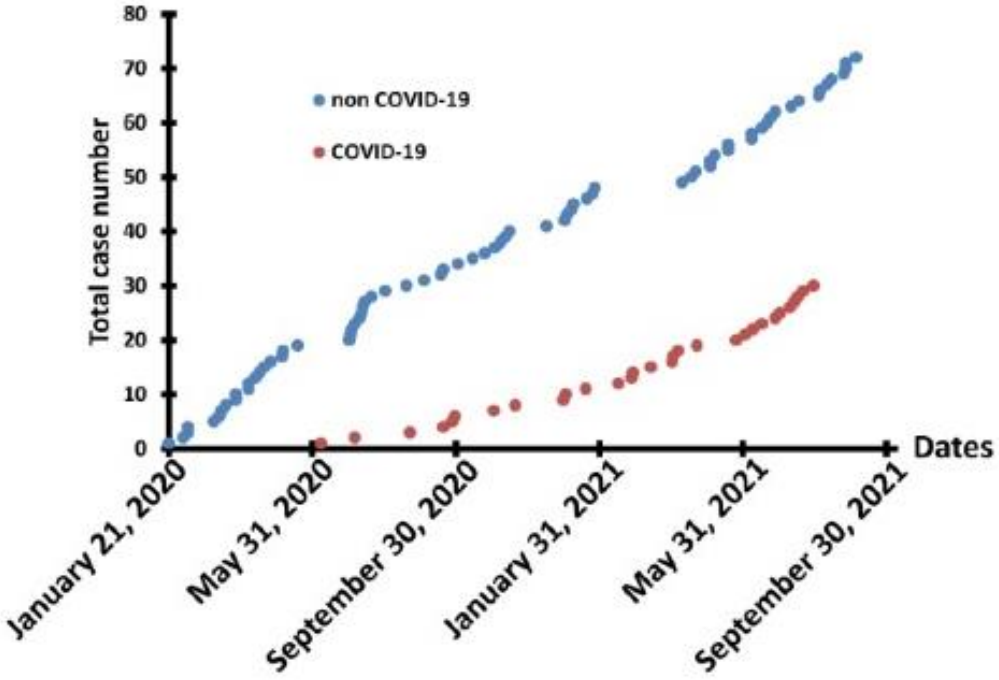
ECMO management

Patients with respiratory failure were considered for ECMO if they had refractory hypoxemia (PaO2<55 mmHg, pulse oximetry oxygen saturations <88%, pH<7.2, despite lung protective mechanical ventilation with plateau pressure < 35, neuromuscular blockade, and prone ventilation as indicated, in accordance with recommendations from the Extracorporeal Life Support Organization (ELSO, www.elso.org). The decision to intitiate ECMO was made by a multidisciplinary ECMO team including pulmonologists, thoracic surgeons, ECMO specialists, and intensivists, using a teleconference line. Different cannulation strategies were used [Internal jugular vein – femoral vein cannulation or predominantly right internal jugular ProtekDuo® cannulation (LivaNova Inc., Pittsburgh, PA, USA)]. The VV-ECMO circuit included Quadrox iD adult (7.0) oxygenator (MAQUET Holding B.V. & Co. KG, Germany) and Rotaflow pump (MAQUET Holding B.V. & Co. KG, Germany). Patients did not receive continuous anticoagulation unless there was clinical and/or radiological evidence of a thrombotic event that warranted its use (eg, DVT, PE, arterial thrombosis). ECMO flow was maintained at least 3.0L/min, consistent with recent reports demonstrating the feasibility of using VV-ECMO without anticoagulation [4-6]. Patient received unfractionated heparin (5,000 U given subcutaneously every 8 hours) for deep venous thrombosis prophylaxis. Thresholds for packed red blood cell transfusion included hemoglobin <7 g/dL or hemodynamic instability in the setting of active blood loss. Platelet transfusion was recommended for platelet counts <50,000/mL, Coagulopathy (INR>2) in the setting of active bleeding was treated with fresh frozen plasma with or without procoagulant factors such as cryoprecipitate.

eFigure 1. Karnofsky Performance Status for COVID-19 and non-COVID-19 Patients Pre- and Post- Lung Transplant



eFigure 2. Cumulative Curve Showing Dates of All Lung Transplants Performed From January 2020 Through September 2021



eTable 1. Clinical Profile of Patients With COVID-19-Associated ARDS on ECMO Support for Greater Than 28 Days.

Variable	Received Lung Transplant (n=17)	Did Not Receive Lung Transplant (n=32)
Age, median (IQR), y	53 (36-59)	52 (45-57)
Women	7 (41.2%)	11 (34.4%)
Men	10 (58.8%)	21 (65.6%)
BMI, kg/m2	27.1 ± 3.9	32.1 ± 4.9
History of smoking	0 (0%)	2 (6.3%)
Hypertension	9 (52.9%)	7 (21.9%)
Diabetes	5 (29.4%)	6 (18.8%)
CKD	0 (0%)	1 (3.1%)
Dialysis	2 (11.8%)	0 (0%)
Chronic Obstructive Pulmonary Disease	0 (0%)	0 (0%)
Laboratory		
Hemoglobin, g/dL	7.7 ± 1	11.7 ± 2
WBC, 1,000/mm3	12 ± 4.8	13.2 ± 6.1
Platelets, 1,000/mm3	180.5 ± 63.8	224.4 ± 110.2
Sodium, mEq/L	142.1 ± 4.4	137.8 ± 4.6
Creatinine, mg/dL	0.6 ± 0.3	1.5 ± 3.7
BUN, mg/dL	26.5 ± 14.7	24.2 ± 12.1
AST, U/L	22.9 ± 18.7	60.6 ± 72.2
ALT, U/L	31.2 ± 22.2	109.5 ± 253.3
Total bilirubin, mg/dL	1.3 ± 1.6	0.6 ± 0.3
Albumin, g/dL	3.3 ± 0.7	2.9 ± 0.5
INR	1.2 ± 0.1	1.1 ± 0.2
ABG (at cannulation)		
pH	7.43 ± 0.1	7.34 ± 0.1
PaCO2	47.3 ± 10.8	58.6 ± 16.3
PaO2	153.2 ± 76.4	91.6 ± 51.2
HCO3	30.8 ± 6	31.6 ± 8.4

Continuous data are shown as means ±standard deviation (SD). BMI, body mass index; BSA, body surface area; CKD, chronic kidney disease (Defined using estimated glomerular filtration rate is less than 60 mL/min); WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, Alanine aminotransferase; INR, international normalized ratio

eTable 2. Patient Characteristics, Intra-operative and Post-operative Findings of COVID-19-Associated ARDS Lung Transplant Recipients

Variable	Age Decade	BMI	Sex	Onset to lung Tx (days)	ICU stay	Ventilator days	Pleural drainage	Post-Op ECMO	Hospital stay	PGD grade1-3	OR time (hours)	Ischemic Time	Intra-Op RBC	Intra-Op FFP	Intra-Op Plt
Patient 1	20s	31.5	Female	40	21	17	14	17	33	YES	8.3	5.3	6	2	3
Patient 2	60s	23.4	Male	114	15	1	24	9	38	YES	9.5	5.0	10	6	1
Patient 3	40s	20.7	Male	91	4	20	23	8	37	YES	10.8	5.1	16	8	4
Patient 4	60s	25.8	Male	49	28	4	61	0	92	NO	9.3	6.0	10	2	2
Patient 5	50s	24.5	Male	65	33	18	20	5	58	YES	9.2	5.3	5	0	0
Patient 6	40s	35.7	Female	75	16	1	13	0	50	NO	10.3	4.4	10	0	3
Patient 7	30s	30.2	Female	87	41	17	31	0	47	YES	10.0	6.0	14	4	2
Patient 8	60s	27.6	Male	143	23	16	17	4	28	YES	11.1	8.1	19	8	2
Patient 9	60s	26.8	Male	89	25	4	29	4	29	YES	9.6	5.6	5	1	0
Patient 10	60s	20.8	Male	314	18	1	13	0	17	YES	7.3	5.6	2	0	0
Patient 11	20s	26.6	Female	87	12	12	15	1	17	NO	8.3	4.9	7	1	1
Patient 12	60s	19.0	Male	300	39	27	39	0	39	YES	8.0	5.7	7	0	0
Patient 13	50s	21.7	Male	90	20	3	20	0	36	NO	9.8	7.0	18	11	8
Patient 14	40s	37.2	Male	252	15	21	19	0	29	YES	8.2	5.9	0	0	0
Patient 15	60s	24.4	Female	170	7	3	14	0	19	NO	9.8	4.8	6	0	0
Patient 16	20s	26.7	Female	164	33	29	25	1	35	YES	8.2	6.0	7	0	1
Patient 17	50s	28.6	Male	116	12	9	21	0	22	YES	11.0	6.3	17	6	3
Patient 18	50s	19.5	Male	169	14	13	17	0	17	YES	8.1	5.4	2	0	0
Patient 19	50s	28.3	Female	92	19	0	32	0	35	YES	10.8	6.1	16	4	2
Patient 20	50s	21.5	Female	170	18	18	18	0	18	YES	9.1	6.5	17	12	5
Patient 21	40s	25.6	Female	199	10	3	10	0	10	YES	8.0	5.9	3	0	0
Patient 22	60s	29.2	Male	175	12	1	19	0	21	NO	7.6	6.6	0	0	0
Patient 23	50s	20.7	Male	126	9	1	10	0	13	NO	8.7	6.1	2	0	0
Patient 24	30s	26.6	Male	43	21	15	19	8	25	YES	9.1	5.8	9	1	2
Patient 25	40s	27.1	Male	75	7	1	10	0	13	NO	8.0	5.8	0	0	0
Patient 26	50s	29.9	Female	239	69	20	44	0	69	YES	7.1	4.7	2	5	0
Patient 27	50s	26.8	Female	85	8	2	15	0	16	YES	6.8	5.0	2	5	0
Patient 28	50s	25.0	Male	95	21	11	20	0	21	YES	7.7	4.8	2	0	0

Patient 29	50s	29.0	Male	78	31	4	4	0	38	YES	7.5	5.2	7	5	3
Patient 30	50s	29.7	Female	485	7	2	19	0	20	NO	6.0	3.8	1	0	0

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