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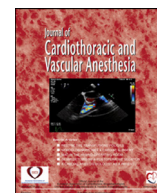
Case Report

Right Ventricular Failure Manifesting in Corona Virus Disease 2019 Acute Respiratory Distress Syndrome: A Call to Transition from Venovenous Extracorporeal Membranous Oxygenation to Right Ventricular Assist Device Extracorporeal Membranous Oxygenation

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Often labeled the forgotten ventricle, the right ventricle's (RV) importance has been magnified over the last 2 years as providers witnessed how severe acute respiratory syndrome coronavirus 2 infection has a predilection for exacerbating RV failure. Venovenous extracorporeal membranous oxygenation (VV-ECMO) has become a mainstay treatment modality for a select patient population suffering from severe COVID-19 acute respiratory distress syndrome. Concomitant early implementation of a right ventricular assist device with ECMO (RVAD-ECMO) may confer benefit in patient outcomes. The underlying mechanism of RV failure in COVID-19 has a multifactorial etiopathogenesis; nonetheless, clinical evaluation of a patient necessitating RV support remains unchanged. Herein, the authors report the case of a critically ill patient who was transitioned from a conventional VV-ECMO Medtronic Crescent cannula to RVAD-ECMO, with the insertion of the LivaNova ProtekDuo dual-lumen RVAD cannula.
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APPROACHING 2 YEARS into the COVID-19 global pandemic, fatigued providers have been tasked with managing a seemingly insurmountable caseload of critically ill patients. Through the utilization of a multidisciplinary approach and adherence to standardized protocols, many institutions have demonstrated gradual improvement in outcomes as clinicians further understand the pathophysiologic basis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The preponderance of right ventricular (RV) failure over left ventricular (LV) failure among severely infected patients stems from the elevated RV afterload with a concurrent decrease in contractility, all presumably secondary to acute respiratory distress syndrome (ARDS), thromboembolic disease, and direct viral penetration.[1] Advanced imaging modalities, including cardiac magnetic resonance imaging and echocardiography, also have shown that the incidence of RV failure exceeds LV failure in critically ill patients with COVID-19.[2,3]

Timely recognition and intervention in the setting of RV compromise are crucial, as these patients can rapidly decompensate. Upon identification of RV failure in a patient already on a conventional venovenous extracorporeal membrane oxygenation (VV-ECMO) circuit, medical therapy in the form of offloading the RV through preload reduction, augmentation of contractility with inotropic agents, and initiation of inhaled pulmonary vasodilators should be optimized.[4] It is when medical therapy yields insufficient and decompensation persists that the option for further mechanical circulatory support be explored. With the advent of a dual-lumen single cannula, such as the LivaNova ProtekDuo, conventional VV-ECMO can be upgraded to further enhance RV support. This report describes a case in which a patient receiving conventional VV-ECMO support for 6 weeks exhibited symptomatic congestive RV failure and underwent internal jugular venous cannula exchange with the insertion of a ProtekDuo right ventricular assist device (RVAD).

Case Report

A 53-year-old man unvaccinated against SARS-CoV-2, with a medical history significant for anxiety, hypertension, and ARDS requiring mechanical ventilation 3 years ago due to substance overdose, presented from the outside facility to the authors' institution for the evaluation of VV-ECMO candidacy (height: 185 cm; weight 98 kg BMI: 29.5 kg/m^2).

In brief, he presented to the previous facility 9 days before transfer to the authors' institution with hypoxic respiratory failure secondary to SARS-CoV-2 infection and was found to be saturating 85% on room air. Contrasted computed tomography (CT) of the chest was performed, revealing expected diffuse bilateral ground-glass opacities. He subsequently was placed on a high-flow nasal cannula and encouraged to self-prone; however, the patient was noncompliant. Thereafter, noninvasive positive-pressure ventilation was provided in the form of bilevel positive airway pressure, with a fraction of inspired oxygen (F_IO_2) set at 100%. The patient initially refused to be intubated, but after 3 days of worsening dyspnea evidenced through shallow, tachypneic respirations, he agreed to proceed. This occurred the day prior to transfer to the authors' facility for VV-ECMO evaluation. Pertinent medical therapy given at the outside facility included 2 doses of 400 mg tocilizumab, 6 mg of dexamethasone daily for 9 days, completion of a 5-day course of remdesivir, and a treatment dose of enoxaparin for a right axillary deep vein thrombus.

On arrival to the authors' center, initial ventilator settings witnessed were set on volume-control continuous mandatory ventilation, an F_IO_2 of 100%, tidal volume of 500 mL, a respiratory rate of 15 breaths/min, and positive end-expiratory pressure at 18 cmH$_2$O. The patient's cardiopulmonary status remained tenuous, evidenced by his arterial blood gas drawn on the aforementioned ventilator settings showing signs of severe hypoxic and hypercapnic respiratory failure in the setting of ARDS shown here: pH of 7.22, PaO$_2$ of 57.8 mmHg, PaCO$_2$ of 61.4 mmHg, and low PaO$_2$/F$_I$O$_2$ ratio of 57.8. He was receiving vasopressor support with norepinephrine at a

fairly high dose of 20 µg/min to prevent hypoperfusion. Cardiothoracic surgery had been notified, and prompt percutaneous VV-ECMO was initiated. This was conducted with a dual-cannula configuration involving one in the right femoral vein (25F) advanced into the abdominal inferior vena cava as the drainage cannula and the other in the right internal jugular vein (22F) as the return cannula, with an initial flow rate of 4.5 L/min per protocol. Cannulae were secured in position, and sterile dressings were applied; the procedure was uncomplicated, and the patient was initiated on anticoagulation with a bivalirudin infusion with coagulation parameters in place. The rate of norepinephrine infusion, initially set at 20 µg/min, was titrated down to 2 µg/min an hour after ECMO initiation. Ventilator settings appropriately were adjusted in accordance with a lung-protective ECMO strategy, utilizing 4-to-6 mL/kg tidal volume and respiratory rate of 10-to-15 breaths/min, per the authors' protocol. Postmembrane arterial blood gas revealed adequate oxygenator performance, with a PaO$_2$/F$_I$O$_2$ ratio of 187. Transthoracic echocardiogram performed after cannulation revealed normal left ventricular ejection fraction 60%-to-65%, normal RV size and function, and normal-appearing tricuspid valve with trace regurgitation appreciated.

He continued supportive care while fine ventilator adjustments were made, and 2 weeks later, a decision was made to transition from a 2-cannula apparatus to a single dual-lumen 27Fr Crescent cannula configuration in the left subclavian vein with simultaneous tracheostomy, with a plan to work with physical therapy and move toward rehabilitation. The transition was performed without complication, and aside from bleeding that was controlled intraoperatively due to the patient being anticoagulated for 2 weeks, he returned to the cardiovascular intensive care unit in a hemodynamically stable condition. The authors attempted to wean from ECMO on multiple occasions; nonetheless, the patient was unable to tolerate a sweep <4 L/min due to hypercapnia, and his CT scan revealing diffusely severe lung disease (Fig 1). He continued undergoing supportive care, physical therapy, and daily awakening. Given significant volume influx through multiple infusions required for sedation, anticoagulation, and inflow from VV-ECMO, the patient was intermittently on loop diuretic infusions as well; however, the authors' focus led to the elimination of multiple infusions with time and implementing oral medications to prevent volume overload.

One morning, a transient bout of hypotension and worsening hypoxia was encountered, and the patient underwent a point-of-care bedside echocardiogram, unveiling septal-D flattening (+McConnell sign) and severely reduced RV function consistent with RV volume overload. Aggressive diuresis was trialed, along with pulmonary vasodilator therapy with epoprostenol, and his course concomitantly was complicated by a suspected nosocomial fungal infection corroborated by a markedly profound leukocytosis and sputum cultures (+) for _Candida Albicans_. The patient was placed on micafungin therapy, with gradual intermittent improvement observed and was noted to be awake, alert, and oriented but extremely weak. Medical therapy for RV failure was pursued until the patient decompensated again 6 weeks into his hospital course,
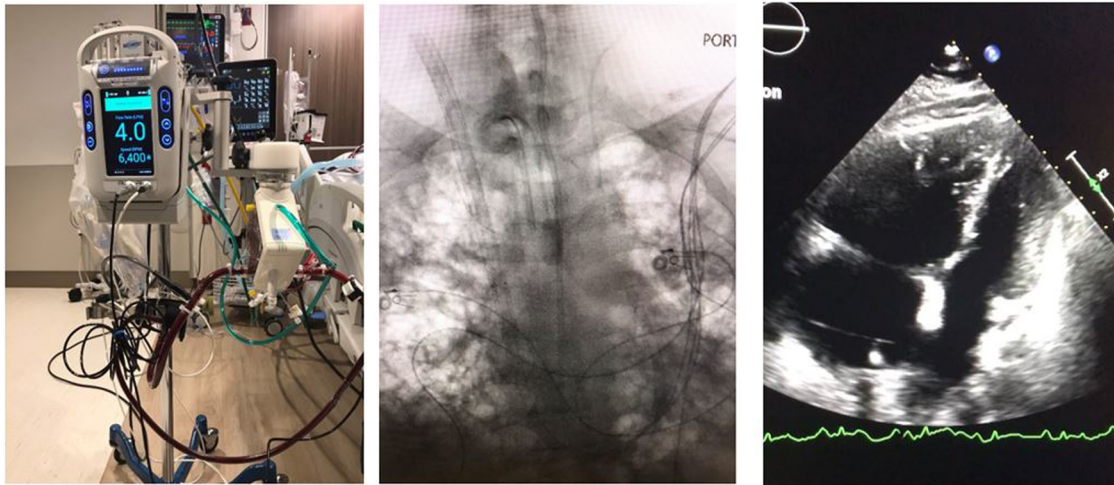
Fig 1. Quadrax-i oxygenator attached to LifeSPARC console with ProtekDuo cannulae seen (left); cannula tip seen entering right PA under fluoroscopy (middle); Echocardiogram image of sepat-D flattening (+McConnell Sign) demanding RVAD (right). PA, pulmonary artery; RVAD, right ventricular assist device.

experiencing a recurrent bout of hypotension and hypoxia in conjunction with marked elevation in liver function tests and rise in creatinine (Table 1). Medications administered included diuresis with furosemide and the initiation of inhaled epoprostenol. At this time, a repeat transthoracic echocardiogram was performed and elucidated just how severe the RV failure was. RV systolic pressure was noted to be 51 mmHg, the RV appeared severely enlarged, and moderate tricuspid regurgitation and elevated pulmonary artery systolic pressure also now accompanied septal flattening visualized 2 weeks prior (Fig 2). At that juncture, a joint decision among all providers was made to exchange the current VV-ECMO Medtronic Crescent dual-lumen cannula for a LivaNova ProtekDuo dual-lumen RVAD cannula, given the severe pulmonary dysfunction evidenced by CT scan and noted lack of reserve.

With the patient receiving VV-ECMO through a single dual-lumen cannula, the complexity of decannulation and substitution with the ProtekDuo RVAD device was not straightforward. A multidisciplinary approach led by the ECMO team was implemented, with all in agreement with establishing drainage through the right femoral vein intraoperatively while concomitantly positioning the Crescent cannula into the subclavian vein to continue inflow. The challenge encountered here was attempting to simultaneously fit 2 32Fr cannulae within the superior vena cava. After accessing the right femoral vein, a dilator kit was utilized to dilate from 8Fr-to-24Fr, until a 25Fr long venous cannula was inserted into the inferior vena cava. The line subsequently was clamped. The Crescent cannula then was clamped, with the drainage remaining attached to the middle port. Under fluoroscopic guidance, the

Table 1
Pertinent Laboratory Studies

Baseline Labs	Values on Arrival	Values Day Before ProtekDuo	Values 1 Month After ProtekDuo	Normal Values
WBC, th/uL	19.9*	25.5*	8.8	4.2-10.8
Hgb, gm/dL	10.7†	7.6†	11.0†	14-18
Platelet, th/uL	198	73†	91†	130-450
Bicarbonate, mmol/L	22	25	30	21-32
BUN, mg/dL	20*	79*	10	7-18
Creatinine, mg/dL	0.6	1.1	0.5	0.6-1.3
Lactate, mmol/L	3.8*	5.9*	1.1	0.4-2.0
Troponin I, ng/mL	0.13	(−)	(−)	≤0.15
NT-proBNP, pg/mL	801*	18,189*	–	0-125
Albumin, gm/dL	2.1†	3.6	3.2	3.4-5.0
Total bilirubin, mg/dL	0.5	3.1*	0.4	0.2-1.0
Protein, gm/dL	5.2	7.9	7.5	6.4-8.2
Alkaline phosphatase, IU/L	116	435*	87	50-136
ALT (SGPT), IU/L	37	3,630*	50	12-78
AST (SGOT), IU/L	35	4,636*	46	15-37

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Hgb, hemoglobin; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; SPGT, serum glutamic pyruvic transaminase; SGOT, serum glutamic-oxaloacetic transaminase; WBC, white blood cell.
  * Pertinent laboratory studies indicate elevated values.
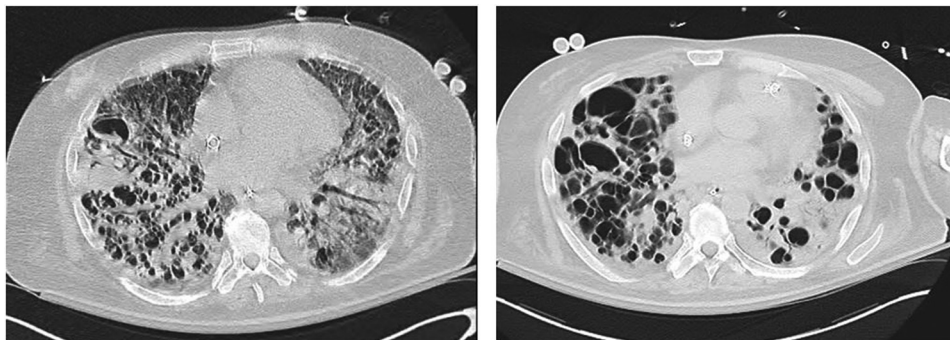 † Pertinent laboratory studies indicate decreased levels.

Fig 2. Severely diffuse dense pulmonary fibrosis secondary to SARS-CoV-2 infection. Left shows Crescent cannula with dual-lumen cannulae seen on patient's left-side. Right shows ProtekDuo cannula with worsened fibrotic changes with dual- lumen cannulae on patient's right side. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

cannula was repositioned into the subclavian vein. VV-ECMO ensued successfully thereafter, and this approach opened adequate room in the SVC for the placement of the ProtekDuo RVAD. Ultrasound-guided access was obtained with a J-wire and exchanged for a 6Fr sheath. A Swan-Ganz catheter was inserted into the right pulmonary artery (PA) thereafter. An extra-stiff Amplatz wire was placed through the Swan-Ganz catheter into the right PA in preparation for dilation. Upon dilation to 26Fr under fluoroscopy, a 31Fr ProtekDuo cannula was inserted. After successful insertion without complications, the RVAD cannula was attached to a separate circuit. This circuit had a Quadrox-i oxygenator linked to a LifeSPARC pump. The patient's saturation increased to 100%, and flow was initiated at 4.5 L at a rate of 7,500 rpm. The patient maintained stability for 15 minutes with isolated RVAD-ECMO configuration saturating >99% SpO$_2$. This was when the subclavian-femoral VV-ECMO was decannulated and removed with adequate pressure maintained to prevent bleeding, along with 3 separate compressive sutures tied with the aid of cardiothoracic surgery. He was transferred back to the cardiovascular intensive care unit hemodynamically stable for further supportive care. In only 24 hours, a significant improvement was observed in renal function, with near-complete resolution of hepatic dysfunction following 2 weeks thereafter. Approximately 1-month postplacement of the ProtekDuo dual-lumen single RVAD cannula (Fig 2), the patient demonstrated resounding improvement in hemodynamic stability and complete resolution of congestive hepatopathy and renal failure as well (Table 1).

Discussion

Much of the data encompassing the cardiovascular complications of COVID-19 mainly have focused on arrhythmias, myocardial dysfunction, and myocardial injury involving the left heart.[5] A recent meta-analysis revealed almost 1 out of 5 patients infected with SARS-CoV-2 exhibit RV dysfunction, with a 3-fold higher likelihood of all-cause death in comparison to subjects without RV failure.[6] The RV is the link between the systemic venous circulation and the pulmonary circuit. Lesser dense myofibrils (approximately one-third density compared to LV) provide a chamber with increased compliance, permitting fluctuations in venous return. Well known, the RV exudes a complex physiologic relationship between rhythm, preload, contractility, afterload, and interdependence with the LV. The supposed mechanism of RV failure in patients with COVID ARDS likely is secondary to dense lung fibrosis leading to increased RV afterload, and pulmonary arterial pressures causing eventual cor pulmonale.[7] Although there likely is multifactorial pathogenesis at play in the setting of COVID, one fact about RV failure irrespective of the underlying cause, is how rapidly patients can decompensate. The medical management of RV failure involves the optimization of preload and mitigating factors that may increase pulmonary vascular resistance. Once inhaled pulmonary vasodilators have been started, a patient's cardiopulmonary status likely is very precarious. This is when a discussion is initiated regarding extracorporeal life support, and whether a patient is an optimal candidate.[8] The indications for initiating ECMO in patients with COVID-19 have been described by Mikkelsen et al, who recommended consideration in patients with PaO$_2$/F$_I$O$_2$ <50 mmHg for ≥3 hours, PaO$_2$/F$_I$O$_2$ <80 mmHg for ≥6 hours, or arterial pH lower than 7.25 with PaCO$_2$ of ≥60 mmHg for 6 hours. The patient met those criteria on arrival to the authors' facility, and RV failure persisted on VV-ECMO, thus demanding the need for isolated RV mechanical circulatory support.

The ProtekDuo had its first in-man use in 2016, in conjunction with the rising popularity of the LV assist device (with primary complications of this device being RV failure).[9] Similar to conventional VV-ECMO, the ProtekDuo operates through centrifugal flow and can provide a flow of up to 4.5 L/min. Upon insertion within the right internal jugular vein, there is a proximal return cannula that remains in the right atrium, while the remainder distal drainage lumen is fed (usually over Swan Ganz catheter) directly into the main pulmonary artery, creating a right atrium-PA bypass tract passing the RV.[10] The advantage of the ProtekDuo cannula in comparison to its competitors is the insertion within the right internal jugular vein, permitting full ambulation within recipients. RVAD-ECMO with the ProtekDuo in patients with COVID-19 in comparison

to mechanical ventilation alone has been shown to reveal no increase in secondary end-organ damage, with higher in-hospital and 30-day survival in the RVAD-ECMO cohort, leading to a conclusion to prioritize RV support in these patients.[11] RVAD-ECMO configuration with the ProtekDuo single dual-lumen cannula, in comparison to conventional Crescent VV-ECMO circuit in severely ill patients with COVID-19, has not yet been studied, though the authors' patient here showcased that there appeared to be a benefit through the addition of RV support.

Conclusion and Follow-Up

The authors presented a case of remarkable hemodynamic improvement status postmechanical circulatory support implementation with the LivaNova ProtekDuo device. Their patient currently is alert, awake, and oriented to person, place, and situation, and is working regularly with physical and occupational therapy. He is off mechanical ventilation, tolerating regular diet, and the authors' plan remains to have him placed at a lung transplant institution once he is able to walk 100-to-200 feet.

Conflict of Interest

None.

References

1 Lan Y, Liu W, Zhou Y. Right ventricular damage in COVID-19: Association between myocardial injury and COVID-19. Front Cardiovasc Med 2021;8:606318.
2 Argulian E, Sud K, Vogel B, et al. Right ventricular dilation in hospitalized patients with COVID-19 infection. JACC Cardiovasc Imaging 2020;13:2459–61.
3 Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging 2020;13:2330–9.
4 Grant C Jr, Richards JB, Frakes M, et al. ECMO and right ventricular failure: Review of the literature. J Intensive Care Med 2021;36:352–60.
5 Tajbakhsh A, Gheibi Hayat SM, Taghizadeh H, et al. COVID-19 and cardiac injury: Clinical manifestations, biomarkers, mechanisms, diagnosis, treatment, and follow up. Expert Rev Anti Infect Ther 2021;19:345–57.
6 Corica B, Marra AM, Basili S, et al. Prevalence of right ventricular dysfunction and impact on all-cause death in hospitalized patients with COVID-19: A systematic review and meta-analysis. Sci Rep 2021;11:17774.
7 Arrigo M, Huber LC, Winnik S, et al. Right ventricular failure: Pathophysiology, diagnosis and treatment. Card Fail Rev 2019;5:140–6.
8 Ventetuolo CE, Klinger JR. Management of acute right ventricular failure in the intensive care unit. Ann Am Thorac Soc 2014;11:811–22.
9 Aggarwal V, Einhorn BN, Cohen HA. Current status of percutaneous right ventricular assist devices: First-in-man use of a novel dual lumen cannula. Catheter Cardiovasc Interv 2016;88:390–6.
10 Nicolais CD, Suryapalam M, O'Murchu B, et al. Use of Protek Duo Tandem Heart FOR percutaneous right ventricular support in various clinical settings: A case series. J Am Coll Cardiol 2018;71(11):A1314.
11 Cain MT, Smith NJ, Barash M, et al. Extracorporeal membrane oxygenation with right ventricular assist device for COVID-19 ARDS. J Surg Res 2021;264:81–9.