Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Mechanical Circulatory Support for the Right Ventricle: The Right Ventricle is No Longer Forgotten

The authors read with great interest the case report by Patel et al. of a patient with severe COVID-19 acute respiratory distress syndrome (ARDS) initially requiring venovenous extracorporeal membrane support (VV ECMO) and subsequently an oxygenated right-ventricular assist device (RVAD).[1] In their report, over the course of ECMO support the patient developed right-ventricular (RV) failure evidenced by septal flattening, McConnell's sign, and severely reduced RV systolic function. Acute RV failure was associated with rising liver function tests, as well as acute renal failure, despite maximal medical therapies to support the RV. At this juncture, the team made the decision to reconfigure the initial VV ECMO strategy to a venopulmonary oxygenated RVAD platform using a Protek Duo Cannula (TandemLife). The Protek Duo cannula, manufactured by Livanova, is a dual lumen cannula that has inflow orifices positioned in the right atrium (RA) and outflow orifices positioned at the distal tip of the catheter in the pulmonary artery (PA). The cannula is then connected to a centrifugal pump. In this configuration, without an oxygenator, the cannula can be used as a percutaneous RVAD, for ventricular support. When an oxygenator is added to the circuit it can be used not only for right ventricular assist but as an ECMO circuit, often referred to as an oxygenated RVAD.

Mechanical circulatory support (MCS) for the RV is an area of intense clinical growth and research. Historically, the RV has persistantly baffled physicians. In 1648 Sir William Harvey writes in *De Motu Cordis*: "Thus the right ventricle may be said to be made for the sake of transmitting blood through the lungs, not for nourishing them."[2] Over time, as cardiac surgery has evolved in arenas such as heart transplantation and left ventricular assist device placement, complex operations have illustrated that acute RV failure remains the Achilles heel in optimal patient survival. Alternatively, clinicians have learned that surgically mimicking a Fontan circulation, with an RV that is bypassed completely, can be done with relatively few short-term sequelae. The question then remains how important the RV is and when should both medical and MCS options be used for acute RV failure. RV failure, in general, is an independent risk factor for morbidity and mortality in a number of clinical conditions including congestive heart failure, ARDS, cardiomyopathies, pulmonary hypertension, and post cardiac surgery.[3,4] The authors are now advancing their understanding of the RV and likely are entering an era where the RV is no longer the "forgotten ventricle."[3,5]

Medical support of the RV includes optimization of the RV afterload with PA vasodilators, optimization of the RV loading with diuretics, and direct RV systolic support with inotropic agents such as epinephrine, milrinone, or levosimendan. After exhausting medical therapies for acute RV failure there are 2 major MCS options: intracorporeal axial flow devices such as the RP Impella (Abiomed, MA) and extracorporeal centrifugal devices with cannulas/grafts that bypass the RV. The vast majority of RV support is temporary. The advantage of the extracorporeal support device includes the ability to introduce an oxygenator. The pulmonary vasculature is exquisitely sensitive to hypoxia and hypercarbia. Both these can be addressed with an inline oxygenator.[6,7] Understanding RV biomechanics and, in particular, the relationship between the RV and PA is key to identifying different phases of RV dysfunction leading to RV failure and death. COVID-19 ARDS has been found to cause acute pulmonary arterial hypertension and RV dysfunction.[7,8] Physiologically, RV/PA coupling is determined by end-systolic and pulmonary arterial elastance.[9] In acute pulmonary hypertensive states, RV contractility increases to maintain RV-PA coupling and the RV elastance to PA elastance ratio remains between 1.5 to 2.[9] In COVID-19 ARDS patients develop systemic inflammation, microvascular thrombosis, hypercapnia, hypoxemia, and acidemia, as well as high driving pressure and mechanical power in those requiring mechanical ventilation. This can result in worsening pulmonary hypertension and reduction in the RV:PA elastance ratio. These factors result in RV dilation, RV systolic failure, and inability to maintain forward flow.[10] For ARDS patients dependent on VV ECMO, preserved RV function is essential. VV ECMO does not support cardiac function; in fact, acute RV failure will result in increased recirculation and hypoxia.

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Several groups have demonstrated successfully the use of oxygenated RVADs in COVID-19 ARDS. Early in the pandemic, Mustafa et al described 40 consecutive patients using the Protek Duo venopulmonary oxygenated RVAD configuration.[11,12] They reported a mortality rate of 17.5% (7 of 40) with the rest of the 33 patients weaned off ECMO. In their cohort, 20 patients were discharged home and 13 patients were discharged to short term rehabilitation.[11,12] Cain et al similarly described 18 COVID-19 ARDS patients with venopulmonary oxygenated RVAD support. In their cohort of patients they had 11.1% (2 of 18) mortality.[10] Both survival outcomes are in sharp distinction from the overall COVID-19 VV ECMO survival that has been published which has ranged from the 16.7% to 65.0%.[13] In a meta-analysis of 1896 patients from 22 studies of VV ECMO support for COVID-19 ARDS the overall mortality was reported to be 37.1% (32.2-42.0). Both of these early papers featuring venopulmonary oxygenated RVAD support demonstrated better survival compared to conventional VV ECMO. This has led many clinicians to believe there may be an indication for RV MCS in COVID-19 ARDS and ARDS in general. To further add evidence that oxygenated RVAD support in COVID-19 ARDS is the optimal cannulation strategy, the most promising data comes from a retrospective multicenter study of adult patients. This study included 435 patients with 99 patients in the oxygenated venopulmonary RVAD configuration and the rest in a VV ECMO strategy.[14] In this study, patients were placed on either platform immediately at the time of initiation. At 90 days there was a survival benefit favoring venopulmonary oxygenated RVAD support with an adjusted hazard rate of 0.52, 95% confidence interval of 0.32 to 0.85, and p = 0.009. In all 3 retrospective studies highlighting venopulmonary RVAD cannulation there was no reported increased risk of pulmonary complications or cannulation complications.

In our own institutional experience, the authors used an oxygenated RVAD for COVID-19 ARDS in 12 patients. The authors found 3 distinct cannulating strategies for these patients. First, we used the Protek Duo RA to PA cannula. Second, the authors used the novel, Spectrum, dual stage, dual lumen, RV, and RA to PA cannula. This cannula was FDA-approved in December 2021. Finally, the authors also used 2 independent cannulas, inflow from the femoral vein, and outflow through a single lumen end hole cannula positioned in the PA from the right internal jugular vein. Having 3 cannulation RV support options was found to increase the armamentarium available to tackle ARDS depending on the clinical situation. Based on the authors' experience and the current literature, a multicenter clinical trial addressing the various cannulation strategies in ARDS should be conducted.

Temporary MCS for the RV is an active area of device development. In addition to the new Spectrum cannula, a new axial flow device is on the horizon designed by Abiomed. Currently, the only axial flow catheter for the right side is the RP Impella. The current iteration of the RP Impella is placed from the right femoral vein. The femoral approach is challenging for RV devices, in particular, due to the difficult in navigating the tricuspid and pulmonary valve from the inferior vena cava as well as the distance. Thus, Abiomed has now developed a 23 French right internal jugular RP Impella. This cannula is positioned in similar fashion as a pulmonary artery catheter and can achieve flows up to 4.0 liters/minute. This axial flow device likely will be used by cardiac anesthesiologists to assist separation from cardiopulmonary bypass in those patients with high risk for acute RV failure or for patients who have isolated RV failure or biventricular failure in the cardiothoracic intensive care unit. Ultimately, this catheter will add to the MCS options available to the cardiac anesthesiologist or cardiac intensivist managing acute RV failure.

Again, we commend the other authors on presenting this unique case report. We are excited to share iown our cannulating platforms with the readership, look forward to implementing platforms of RV MCS in the near future, and eagerly anticipate clinical trials that demonstrate the noninferiority of venopulmonary oxygenated RVAD support in ARDS.

Conflict of Interest

None.

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