When to consider lung transplantation for COVID-19

Hop Foch/Phanie/Science Photo Library

Lancet Respir Med 2020

Published Online
August 25, 2020
https://doi.org/10.1016/S2213-2600(20)30393-3

See Online/Case Report
https://doi.org/10.1016/S2213-2600(20)30361-1

Several respiratory viruses are known to cause acute respiratory distress syndrome (ARDS). Survival and lung recovery rates are well known for influenza viruses; however, ARDS related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has posed an unprecedented challenge. Lung transplantation has been offered as a life-saving therapy for some patients with COVID-19 who have presented with persistent lung failure despite several weeks or months of support in the intensive care unit (ICU). To date, only a handful of cases have been reported via the media or scientific reports.[1] In these initial reports, early outcomes have been acceptable for this severely ill group of patients. As a high-intensity therapy in the context of a new disease, publication bias is also expected to occur—more cases have probably been seen but not reported because of poor outcomes.

In *The Lancet Respiratory Medicine*, Christian Lang and colleagues[2] provide an excellent report of a very sick 44-year-old patient with COVID-19-associated ARDS, who was treated with a life-saving lung transplantation. As a team at one of the centres with the most experience in extracorporeal membrane oxygenation (ECMO) bridge and high-risk lung transplantation in Europe, they provide a meticulous and multidisciplinary transplant assessment process before embarking on this therapy. Even so, transplanting a patient who had been immobile for several weeks without first-person consent did carry important risks and, not unexpectedly, these were reflected in a prolonged ICU and hospital stay after the procedure.

Although potentially life saving, the true effect of lung transplantation in the acute setting of COVID-19 is likely to be small. Most patients who progress to severe lung failure have comorbidities that preclude them from being transplant candidates. Moreover, many will develop secondary complications such as renal dysfunction, muscle wasting, or other organ failure while on ECMO. Advanced age is also a contraindication to lung transplantation in this setting. Thus, prevention of COVID-19 infection remains the best strategy to save lives.

We list here ten considerations that we believe should be carefully weighed when assessing a patient with COVID-19-associated ARDS regarding potential candidacy for lung transplantation. The following factors are likely to increase the chance of a positive outcome.

First, candidates should be younger than 65 years. Existing experience from ECMO bridge to lung transplantation shows poorer outcomes for older patients.

Second, candidates for transplantation should have only single-organ dysfunction.

Third, sufficient time should be allowed for lung recovery. It is in the best interests of the patient to be able to survive without a transplant given the suboptimal long-term survival rates of lung transplantation (about 60% at 5 years). Previous observations have shown that lungs that are severely injured from influenza or bacterial pneumonia can recover to support life with non-limiting function after several weeks to months on ECMO and complete absence of organ function.[3] Whether COVID-19 will have a recovery rate inferior to that of other infectious agents remains unknown. Data from France have shown a recovery rate for patients with COVID-19-related ARDS on ECMO similar to that for patients with ARDS due to other causes.[4] Although no guideline yet exists, it is our opinion that transplantation should not be considered less than 4–6 weeks after initial clinical signs of respiratory failure.

Fourth, there should be radiological evidence of irreversible lung disease, such as severe bullous destruction or evidence of established fibrosis.

Fifth, the patient should be awake and able to discuss transplantation. Transplantation in patients with ARDS has often occurred without first-person consent. Patients need to understand the impact of transplantation on quality of life. Becoming acutely ill with a respiratory illness and waking up after a lung transplant with a life of immunosuppression and complications ahead can be psychologically traumatic and sometimes insurmountable.

Sixth, patients should be able to participate in physical rehabilitation while on the transplantation waiting list. Data from ECMO bridge to transplant clearly show improved outcomes in such patients.[5,6]

Seventh, patients should fulfil the remaining typical criteria for transplantation; for example, adequate

body-mass index and absence of other notable comorbidities, such as severe coronary artery disease.[7]

Eighth, the patient should have a recent negative SARS-CoV-2 PCR result, or infectivity assays using deep respiratory tract samples showing absence of viable virus. Evidence shows that mortality after surgical procedures is significantly higher for PCR-positive patients, even in those who are asymptomatic.[8]

Ninth, the transplantation centre should have substantial experience with high-risk transplantation. Lung transplantation in patients on ECMO bridging for ARDS are some of the highest-risk and most complex procedures. As such, only centres with substantial experience in ECMO bridging should offer the procedure. To that end, referral to a few specialised centres could greatly improve outcomes for patients with COVID-19 who undergo lung transplantation.

Tenth, the centre should have access to a broad donor pool and low waiting-list mortality. This factor will maintain fair and equitable donor organ allocation and provide the chance for life-saving organ transplantation to patients who are more likely to survive.

Another consideration will be whether patients who recover from severe COVID-19-related ARDS and leave hospital will ultimately develop chronic lung dysfunction related to post-COVID-19 pulmonary fibrosis.[9] Although none of the reported transplants has been done in that scenario, with time and more experience of the longer-term effects of COVID-19, a population of patients who have developed fibrosis might require transplantation.

In summary, with ECMO support, patients with severe, life-threatening lung failure secondary to ARDS can be treated for remarkably long periods and return to meaningful and active lives. SARS-CoV-2 has caused a worldwide pandemic of unprecedented magnitude, with COVID-19 leading to ARDS in many patients. The underlying mechanism of COVID-19-induced lung injury, its associated systemic comorbidities, and its recoverability are still incompletely understood at this time. As such, lung transplantation should be considered only in a very select group of patients with COVID-19-related ARDS. The ultimate effect and results of offering this life-saving therapy in this population remain unknown.

We declare no competing interests.

Marcelo Cypel, Shaf Keshavjee
marcelo.cypel@uhn.ca

Division of Thoracic Surgery, Department of Surgery, University Health Network, University of Toronto, Toronto Lung Transplant Program, Toronto, ON M5G 2C4, Canada

1 Chen J-Y, Qiao K, Liu F, et al. Lung transplantation as therapeutic option in acute respiratory distress syndrome for coronavirus disease 2019-related pulmonary fibrosis. *Chin Med J (Engl)* 2020; **133:** 1390–96.

2 Lang C, Jaksch P, Hoda MA, et al. Lung transplantation for COVID-19-associated acute respiratory distress syndrome in a PCR-positive patient. *Lancet Respir Med* 2020; published online Aug 25. https://doi.org/10.1016/S2213-2600(20)30361-1.

3 Luyt C-E, Combes A, Becquemin M-H, et al. Long-term outcomes of pandemic 2009 influenza A(H1N1)-associated severe ARDS. *Chest* 2012; **142:** 583–92.

4 Schmidt M, Hajage D, Lebreton G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med* 2020; published online Aug 13. https://doi.org/10.1016/S2213-2600(20)30328-3.

5 Benazzo A, Schwarz S, Frommlet F, et al. Twenty-year experience with extracorporeal life support as bridge to lung transplantation. *J Thorac Cardiovasc Surg* 2019; **157:** 2515–25.e10.

6 Hoetzenecker K, Donahoe L, Yeung JC, et al. Extracorporeal life support as a bridge to lung transplantation—experience of a high-volume transplant center. *J Thorac Cardiovasc Surg* 2018; **155:** 1316–28.e1.

7 Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014—an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 2015; **34:** 1–15.

8 Doglietto F, Vezzoli M, Gheza F, et al. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. *JAMA Surg* 2020; published online June 12. https://doi.org/10.1001/jamasurg.2020.2713.

9 Spagnolo P, Balestro E, Aliberti S, et al. Pulmonary fibrosis secondary to COVID-19: a call to arms? *Lancet Respir Med* 2020; **8:** 750–52.