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## **Lung transplantation for patients with severe COVID-19-related ARDS in Korea**

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Lung transplantation is the gold standard for end-stage chronic lung diseases and could be a salvage therapeutic option even in acute respiratory distress syndrome (ARDS). The coronavirus disease 2019 (COVID-19) mainly affects the respiratory system with some patients rapidly progressing to ARDS. Some patients with COVID-19-related ARDS who require MV progress to the ARDS fibrotic phase, which is associated with increased mortality. Therefore, based on the experience obtained during previous respiratory virus outbreaks, extracorporeal membrane oxygenation (ECMO) could be used to bridge such patients to recovery or lung transplantation. Although lung transplantation has been suggested as a salvage therapy for carefully selected patients with ARDS, however, a limited experience on this potentially life-saving procedure for COVID-19-related ARDS was noted. Last year, sporadic cases of lung transplantation for patients with COVID-19-related ARDS were reported and bridging of patients to lung transplantation with ECMO is being used increasingly with growing success. Recently, a case series of patients with COVID-19-related ARDS who were bridged to lung transplantation by ECMO at high-volume centers in four Western countries shows that LT could be done successfully with good early post-transplantation outcomes. In Korea, eleven consecutive lung transplants for patients with severe COVID-19-related ARDS between June 2020 and June 2021 were retrospectively analyzed. The median age was 60.0 years (interquartile range [IQR], 57.5–62.5 years; six males). All patients were supported with veno-venous ECMO at lung transplantation listing and received rehabilitation at a median of 28.0 (IQR, 17.5–43.0) days before lung transplantation. Patients were transplanted at a median of 49 (IQR, 32–66) days after ECMO cannulation. Primary graft dysfunction within 72 h of lung transplantation developed in two (18.2%) patients. Major postoperative complications were infection and bleeding requiring interventions in seven (63.5%) and four (36.4%) patients, respectively. One patient expired 4 days after lung transplantation due to sepsis and one patient underwent re-transplantation for graft failure. After a median follow-up of 155 (IQR, 144–225) days, 10 patients are alive and recovering well. Lung transplantation in patients with COVID-19-related ARDS leads to acceptable short-term outcomes in Korea. Therefore, lung transplantation could be considered only for patients with reserved physical function as experienced from previous

ARDS patients in Korea. However, lung transplantation for ARDS or COVID-19 raises medical issues. Although alveolar regeneration after acute lung injury is still poorly characterized, the lung has vast potential to repair and regenerate damaged cells after injury. Within the last decade, the use of ECMO in ARDS has increased significantly and this allows the lungs to recover by reducing additional injury by the mechanical ventilation, resulting in anecdotal reports of native lung recovery after prolonged ECMO support. Therefore, considering the inadequate post-transplantation survival outcome, and that use of lifelong immunosuppressant is required, it is worthwhile to wait for expected recovery rather than undergo this major operation. In addition, several concerns including concomitant infections and uncertainty of long-term outcomes limit the use of lung transplantation as a salvage therapy for patients with severe COVID-19-related ARDS. Furthermore, there is an ethical dilemma. Transplantation for irreversible lung disease is characterized by a global shortage of donor organs. Patients with a good prognosis can die on the waiting list. Accepting high-urgency candidates with COVID-19-related ARDS during the pandemic will disadvantage patients on the waiting list, increase waiting-list mortality, decrease post-transplantation survival, and distort the discriminatory capacity of lung allocation systems. Given the high mortality of patients with COVID-19-related ARDS on ECMO, lung transplantation could be considered an option, but should be considered only in a very select group of patients with COVID-19-related ARDS. Several considerations that should be carefully evaluated when assessing a patient with COVID-19-related ARDS regarding potential candidacy for lung transplantation, if the patient were confirmed negative conversion of virology status by performing consecutive nucleic acid tests with multiple respiratory samples. Most of all, sufficient time should be allowed for lung recovery. Previous observations have shown that lungs that are severely injured from influenza or bacterial pneumonia can fully recover after several weeks to months on ECMO. In addition, recent 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. Therefore, it is in the best benefits of the patient to be able to survive without a transplant given the suboptimal long-term survival rates of lung transplantation. In addition, there should be radiologic evidence of irreversible lung disease with computed tomography, although alveolar regeneration after acute lung injury is still poorly characterized. Second, patients should be able to participate in physical rehabilitation while on the ECMO support and the transplantation waiting list. Data from ECMO bridge to lung transplantation clearly demonstrate improved outcomes of transplant results for these patients. More details of these and other considerations will be discussed in the symposium. Suggested Readings

1. Lung transplantation for acute respiratory distress syndrome: A multicenter experience. *Am J Transplant*. 2021 Jul 13. doi: 10.1111/ajt.16759. Online ahead of print.
2. Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries. *Lancet Respir Med*. 2021 May;9(5):487-497.
3. When to consider lung transplantation for COVID-19. *Lancet Respir Med*. 2020 Oct;8(10):944-946.
4. Lung transplantation for severe COVID-19-related ARDS. *Ther Adv Respir Dis*. 2022 Jan-Dec;16:17534666221081035.

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5. Lung Transplantation in Patients With COVID-19-The Early National Experience. *Semin Thorac Cardiovasc Surg.* 2022 Aug 28;S1043-0679(22)00210-6 (in press).
6. A Matched Survival Analysis of Lung Transplant Recipients with Covid-19-related Respiratory Failure. *Ann Thorac Surg.* 2022 Oct 10;S0003-4975(22)01314-5 (in press).
7. Lung Transplant for ARDS after COVID-19: Long-Term Outcomes and Considerations about Detrimental Issues. *J Clin Med.* 2022 Aug 15;11(16):4754.
8. Extracorporeal membrane oxygenation support in adult patients with acute respiratory distress syndrome. *Expert Rev Respir Med.* 2020 May;14(5):511-519.