Extracorporeal Life Support in Lung Transplantation

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KEYWORDS

• Extracorporeal membrane oxygenation • ECMO • Lung transplantation • Mechanical ventilation
• Bridge to transplant • Cardiopulmonary bypass • Primary graft dysfunction

KEY POINTS

- Advances in extracorporeal life support technology, patient selection, and management have led to improvements in outcomes for select transplant patients.
- Strategies that help maximize pretransplant conditioning and improve posttransplant outcomes in extracorporeal membrane oxygenation (ECMO)–supported patients include minimization of sedation, avoidance of endotracheal intubation, and early mobilization (facilitated by upper-body cannulation configuration).
- Successful ECMO bridge to transplant remains challenging, highlighting the need for both careful patient selection and anticipatory planning for potentially difficult end-of-life scenarios.
- ECMO may provide hemodynamic support comparable with cardiopulmonary bypass during lung transplant with a more favorable risk-benefit profile.
- ECMO may facilitate allograft recovery in severe forms of primary graft dysfunction by correcting refractory hypoxemia, providing right ventricular support, and minimizing potential for ventilator-associated lung injury.

INTRODUCTION

Patients with end-stage respiratory failure who are candidates for lung transplant often need invasive mechanical ventilation (IMV) to support gas exchange. However, transplant candidates supported with IMV have traditionally had worse posttransplant outcomes than those not requiring pretransplant IMV, often resulting in transplant centers deeming such patients ineligible for active listing.[1] Extracorporeal life support (ECLS), most often referred to as extracorporeal membrane oxygenation (ECMO), has the ability to serve as a bridge to transplant (BTT) for patients in whom IMV is insufficient to maintain adequate gas exchange, although this approach has also historically been associated with poor posttransplant outcomes.[2,3] In a study of all lung transplants performed in the United States between 1987 and 2008, the use of IMV and ECMO pretransplant was associated with significantly higher mortality (adjusted hazard ratios for death of 1.49 and

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2.55, $P<.0001$, respectively) compared with unsupported patients.[2] Differences in outcomes for mechanically supported patients can be attributed, at least in part, to higher pretransplant severity of illness and deconditioning from immobility. IMV carries the risk of ventilator-associated complications, whereas suboptimal timing of ECMO initiation and circuit-associated complications (eg, hemorrhage and thrombosis), particularly with earlier generations of ECLS technology, have contributed to poor transplant outcomes.[2,4] However, in the context of improved risk-benefit profile of extracorporeal technology,[5,6] advances in cannulation strategies,[7,8] and changes in both patient selection and management during ECMO support,[4,9–16] recent data suggest that ECMO as BTT is a viable strategy for carefully selected transplant candidates.[4,9,17,18]

- The use of ECMO pretransplant has traditionally been associated with poor posttransplant outcomes.
- Advances in extracorporeal technology, patient selection, and management during ECMO support have led to improved outcomes in select transplant candidates.

INDICATIONS AND PATIENT SELECTION

Extracorporeal Membrane Oxygenation as Bridge to Transplant

Appropriate patient selection and timing of ECMO initiation remain crucial aspects of achieving success with ECMO as BTT.[19] However, there are no randomized controlled trials evaluating which patients with end-stage lung disease are most likely to benefit from ECMO in this setting. Candidates with the highest predicted pretransplant mortality, who in turn receive the highest priority for transplant in the current lung allocation system,[20] are often the ones with the greatest degree of impairment in oxygenation and ventilation and would benefit most from the gas exchange support of ECMO. However, those who are too critically ill at the time of consideration for ECMO may no longer be appropriate candidates for transplant, and thus are deemed inappropriate for ECMO support. The 2015 International Society for Heart and Lung Transplantation consensus document on selection of lung transplant candidates outlines several patient characteristics for which ECLS is recommended, including young age, absence of multiorgan dysfunction, and good rehabilitation potential.[21] Recommendations against ECLS as BTT include septic shock, multiorgan dysfunction, severe arterial occlusive disease, heparin-induced thrombocytopenia, prior prolonged mechanical ventilation, advanced age, and obesity. Because physical deconditioning is considered by many centers to be a strong relative contraindication to transplant eligibility, ECMO may be considered as a means of optimizing participation in physical therapy before the development of significant debility.[9,18] Likewise, patients with end-stage respiratory failure associated with severe pulmonary arterial hypertension are at high risk for sudden onset of hemodynamic collapse,[22,23] a risk that may be mitigated by the timely use of ECMO.[24,25]

- Patients who may derive the greatest benefit from ECMO as BTT are those with cardiopulmonary impairment severe enough that it limits their ability to maintain the physical conditioning necessary to tolerate transplant.

Although it is important to initiate ECMO before the development of contraindications to transplant, ECMO itself may introduce the risk of important pretransplant complications, including hemorrhage with the need for blood transfusion, which, in turn, may cause allosensitization to donor antigens and limit the availability of suitable lung allografts.

The optimal timing of ECMO initiation remains an area of uncertainty and is subject to the practice and experience of individual transplant centers. Its timing may also be influenced by the anticipated wait times for transplant within each donor service area.[26,27] Likewise, patient demographics and disease-specific factors have an important impact on the likelihood of survival to transplant and can help inform patient selection and timing of ECMO as BTT. For instance, short stature has been associated with a 34% lower rate of transplant and 62% higher rate of death or removal from the transplant waiting list because of clinical deterioration compared with candidates of average stature,[28] whereas higher levels of N-terminal pro–B-type natriuretic peptide in patients with pulmonary arterial hypertension have been associated with an increased risk of death or transplant.[29] Algorithms for patient selection have been proposed,[26,30,31] although more data, including prediction models, are needed to identify patients who are most likely to benefit from ECMO and to determine the optimal timing of its initiation.

- Factors affecting transplant waiting times should be factored into the decision of whether and when patients should undergo ECMO as BTT in order to help balance the risks and benefits of providing pretransplant ECMO support.