Extracorporeal membrane oxygenation as a bridge to lung transplantation in a Turkish lung transplantation program: our initial experience

Mustafa Vayvada · Yesim Uygun · Sevinc Citak · Ertan Saribas · Atakan Erkiliç · Erdal Tasci

Received: 15 May 2020 / Accepted: 12 August 2020 / Published online: 27 August 2020
© The Japanese Society for Artificial Organs 2020

Abstract
Lung transplantation is a life-saving treatment for patients with end-stage lung disease. Although the number of lung transplants has increased over the years, the number of available donor lungs has not increased at the same rate, leading to the death of transplant candidates on waiting lists. In this paper, we presented our initial experience with the use of extracorporeal membrane oxygenation (ECMO) as a bridge to lung transplantation. Between December 2016 and August 2018, we retrospectively reviewed the use of ECMO as a bridge to lung transplantation. Thirteen patients underwent preparative ECMO for bridging to lung transplantation, and seven patients successfully underwent bridging to lung transplantation. The average age of the patients was 45.7 years (range, 19–62 years). The ECMO support period lasted 3–55 days (mean, 18.7 days; median, 13 days). In seven patients, bridging to lung transplantation was performed successfully. The mean age of patients was 49.8 years (range 42–62). Bridging time was 3–55 days (mean, 19 days; median, 13 days). Two patients died in the early postoperative period. Five patients survived until discharge from the hospital. One-year survival was achieved in four patients. ECMO can be used safely for a long time to meet the physiological needs of critically ill patients. The use of ECMO as a bridge to lung transplantation is an acceptable treatment option to reduce the number of deaths on the waiting list. Despite the successful results achieved, this approach still involves risks and complications.

Keywords • Extracorporeal membrane oxygenation • Lung transplantation • End-stage lung disease

Introduction
Lung transplantation is an effective and safe treatment option for patients with end-stage lung disease and is widely used worldwide. The condition of patients on the waiting list for lung transplantation may deteriorate because their condition is not favorable for survival until a suitable donor is found (1). These patients are generally followed up with mechanical ventilatory support in intensive care units (ICUs). However, mechanical ventilation may increase the risk of acute respiratory failure and hemodynamic instability; further, ventilator-associated pneumonia and lung damage may occur. Even if an optimal strategy is used for mechanical ventilation-based therapy, there may be a high risk of developing refractory hypercapnia and/or hypoxia (2). This may be associated with high mortality before and after lung transplantation due to organ failure. Reportedly, post-transplant mortality rates were significantly higher in patients who were bridged to lung transplantation using mechanical ventilation than in those without mechanical ventilatory support (3). Extracorporeal life support systems provide the only chance to these patients to survive until a suitable donor is found. These systems reduce morbidity and provide support according to the physiological needs of patients. Extracorporeal membrane oxygenation (ECMO)
prevents patient deterioration and helps patients attain a better condition until a suitable donor is found.

Owing to the increased morbidity and poor survival associated with hemolysis, infection, hemorrhage, and hemodynamic instability resulting from the use of ECMO, at many transplant centers, its use during the preoperative period is considered a relative contraindication. However, good outcomes obtained with ECMO used as a salvage therapy for primary graft dysfunction after lung transplantation increased the interest in ECMO again (4). Upon improvements in lung transplantation results, with appropriate patient selection, ECMO use can act as a bridge to transplantation in these patients (5). Recent advancements in hollow fiber, polymethylpentene oxygenators, new-generation centrifugal pumps, more durable circuits, and heparin-coated surfaces have increased the use of ECMO as a bridge to lung transplantation (6). According to the 2014 consensus report of the International Association of Heart and Lung Transplantation, the use of ECMO as a bridge to lung transplantation is recommended in young patients without multiorgan failure and with good potential for rehabilitation (7).

With the use of ECMO as a bridge to lung transplantation, the number of patients undergoing lung transplantation and achieving overall survival has increased. At many different centers, patients who were bridged to lung transplantation with ECMO have achieved better survival outcomes than their counterparts (4–9). In Turkey, bridging to lung transplantation is a relatively new concept and data on the use of ECMO as a bridge to lung transplantation are very limited. In this article, we present our initial experience with the use of ECMO as a bridge to lung transplantation.

**Materials and methods**

In this study, we retrospectively examined the use of ECMO as a bridge to lung transplantation between December 2016 and August 2018 at the Kosuyolu Yüksek İhtisas Training and Research Hospital, Istanbul, Turkey. During this period, 55 patients underwent lung transplantation, and 34 patients who were candidates for lung transplantation died on the waiting list. In addition, 13 patients preoperatively required ECMO, and 7 patients were successfully bridged to lung transplantation (1/4 in 2016, 3/26 in 2017, and 3/25 in 2018). The acceptance rate of donors who offered to donate their lungs at our center was 23% (55/239). The median waiting time for patients who underwent lung transplantation was 97 (range, 3–427) days, whereas the median waiting list mortality time was 50 (range, 8–338) days. ECMO was performed for 6 of the 34 patients who died on the waiting list. The other patients on the waiting list deteriorated due to acute exacerbation of the disease or infection at an external center, because of which ECMO could not be performed. Therefore, these patients were not transferred to our hospital.

The decision to perform ECMO was made by a team of thoracic surgeons, intensive care specialists, and transplant chest disease specialists. Pre-ECMO details have been provided in Table 1. The main indications for the use of extracorporeal support before lung transplantation were persistent hypercapnia and/or hypoxic respiratory failure (PCO₂ > 80 mmHg, P/F < 80 mmHg). ECMO was performed within the initial 48 h in patients in whom no response was observed despite optimal mechanical ventilation or in those with poor pulmonary reserve who could not be taken off mechanical ventilation. Regarding patient selection, not only patients on the waiting list but also those with acute deterioration at an external center were taken into consideration. Factors such as age, diagnosis of the underlying lung disease, comorbidities, absence of multiorgan failure, adaptation to post-transplant rehabilitation, neurological status and absence of active bacteremia were taken into account for patient selection. Patients under the age of 60 were considered candidates for ECMO as a bridge to lung transplantation; however, patients over the age of 60 who can good rehabilitation and have minimal medical and surgical problems were also considered candidates.

After cardiologic evaluation, 1 patient underwent venoarterial (VA) ECMO due to right heart failure and hemodynamic instability, whereas 12 patients underwent veno-venous (VV) ECMO. Under the ECMO cannulation strategy, cannula diameter was selected so as to achieve a minimum blood flow rate of 5 L/min. Two patients were cannulated with the bivacal dual-lumen cannula. The jugular and femoral veins were cannulated in 10 patients. Right subclavian artery–femoral vein cannulation was performed in 1 patient who required VA ECMO and in 2 patients who were followed up with VV ECMO due to the development of hemodynamic instability.

Extubation was planned in patients with hemodynamic and respiratory improvement after the application of ECMO. Sedatives and paralytic drugs were not administered to keep patients awake and to enable them to perform active physiotherapy. Tracheostomy was performed within the initial 48 h in patients who could not tolerate extubation or who needed frequent aspiration and bronchoscopy such as those with cystic fibrosis. In non-extubated patients, early tracheostomy was performed using mechanical ventilatory support to the minimum and satisfying physiological needs such as drinking and eating.

The goal of ECMO support was to ensure that patients were awake and comfortable; pH was maintained between 7.35 and 7.45; saturation was maintained at 85–90%; and patients were capable of spontaneous breathing, feeding, and mobilization. Patients in whom these goals could not be achieved were not included in the lung transplant waiting list. Erythrocyte suspension and platelet transfusion were performed to achieve a hemoglobin level of 10–12 mg/dl and platelet
count of >50,000/μl. The target activated clotting time was 160–180 s in VV ECMO and 180–200 s in VA ECMO during coagulation follow-up.

In immunosuppressive treatment after transplantation, in addition to triplet therapy comprising tacrolimus, mycophenolate mofetil, and prednisolone, induction therapy with 20 mg basiliximab was administered on the day of transplant and post-transplant 4 days.

### Results

During the study period, 13 patients underwent ECMO as a bridge to lung transplantation. The average age of these patients was 45.7 (range, 19–62) years. The most common cause for receiving ECMO as a bridge to lung transplantation was idiopathic interstitial pneumonia (IIP) \( (n = 8) \). Other etiologies included adenocarcinoma (lepidic adenocarcinoma/incidental adenocarcinoma with mixed subtypes; \( n = 2 \)), cystic fibrosis \( (n = 2) \), and chronic obstructive pulmonary disease \( (COPD; n = 1) \). The ECMO support period lasted 3–55 (average, 18.7; median, 13) days. Three of the 13 patients were on the waiting list. The condition of these 3 patients worsened during the examination for...
Patients who did not undergo transplantation

In 6 of the 13 patients, bridging to lung transplantation was not successful. The average age of these patients was 41 (range, 19–52) years. Their diagnoses included cystic fibrosis \((n=2)\), IIP \((n=3)\), and COPD \((n=1)\). The ECMO support period lasted 10–32 days (average, 19.6 days; median, 21 days). Two patients were on the waiting list, whereas 4 were accepted from an external ICU. Two patients with cystic fibrosis died of sepsis on the 21st and 28th days of ECMO support. Both of these patients received prophylactic antibiotics according to the previous colonization.

In 1 patient who was followed under ECMO for 28 days, VV ECMO was converted to VA ECMO due to hemodynamic instability on the 25th day of ECMO support. In 1 of the 2 patients with interstitial lung disease, VA ECMO was performed directly because of pulmonary hypertension and right heart failure. The other patient developed right heart failure within the initial 24 h of VV ECMO implantation. Therefore, VV ECMO was converted to VA ECMO. These 2 patients died on the 11th and 16th days due to acute cardiac failure. The 1 patient who was diagnosed with interstitial lung disease was placed on VV ECMO and followed up without the requirement for mechanical ventilation from the 1st day; this patient died on the 32nd day due to cerebral hemorrhage. The patient with COPD died of cardiac arrest of unknown cause on the 10th day of follow-up with VV ECMO.

Remarkably, patients who did not undergo transplant were younger than those who did. The main difference between the two groups with similar preoperative features was the use of a double-lumen cannula. The main cause of failure was prolonged immobility on ECMO, particularly in the 2 young patients with cystic fibrosis.

Patients who underwent transplantation

In 7 out of the 13 patients, bridging to lung transplantation was performed successfully. Two of these patients underwent double-lumen cannulation through the right internal jugular vein. In these patients, tracheostomy was performed because extubation could not be performed within 48 h and there was no requirement for mechanical ventilation. Jugular vein–femoral vein cannulation for VV ECMO was performed in the other 5 patients.

The average age was 49.8 (range, 42–62) years. Bridging time was 3–55 days (average, 19 days; median, 13 days). IIP was diagnosed in 5 patients. One patient was diagnosed with lepidic-type adenocarcinoma, and 1 who was diagnosed with IIP had undergone lung transplantation; however, the definitive pathology in this patient was reported to be mixed-type adenocarcinoma.

Clamshell incision was performed in all patients. For hemodynamic stability during the perioperative period, VV ECMO was converted to central VA ECMO because the aorta and right atrium could be directly visualized. Bilateral lung transplantation was performed in 6 patients and single (right) transplantation in 1 patient. The average ischemia time was 262 (range, 180–360) min for single lung transplantation and 414 (range, 290–520) min for bilateral lung transplantation. The average number of red blood cell (RBC) transfusions was 11.2 (range, 6–26) units during the perioperative period and postoperative day 1. All patients exhibited good respiratory parameters and hemodynamic stability after lung transplantation; thus, ECMO support was terminated. The characteristic features of donor lungs are presented in Table 2.

Overall, 5 of the 7 patients survived to discharge from the hospital. Two patients died during the early postoperative period. Both patients were more than 60 years old. The first patient with idiopathic pulmonary fibrosis had bilateral lung transplantation on the 3rd day of ECMO support. There were no complications at the intraoperative and early postoperative period. Bacteremia was not

Table 2  Donor characteristics

| Donor age, year | 29.4 (16–52) |
|----------------|-------------|
| Cause of death |            |
| Intracerebral hemorrhage | 2 |
| Subarachnoid hemorrhage | 2 |
| Head injury | 1 |
| Dilated cardiomyopathy | 1 |
| Hanging (suicide) | 1 |
| ≥ 20 pack-year smoking | 4/7 |
| Donor intubation, day | 4.1 (1–8) |
| Donor P/F ratio | 374 (278–406) |
| Donor lung ischemic time | 248.8 (180–350) |
identified when offered suitable donors, but the production of preoperative blood culture was positive. The patient died on the 20th postoperative day due to sepsis. The second patient with COPD had bilateral lung transplantation was performed on the 13th day of ECMO support. Massive blood transfusion was required perioperatively due to intense adhesions. ECMO support was terminated at the end of the operation due to good respiratory parameters and hemodynamic stability. However, the patient developed primary graft dysfunction in the 20th h, for which postoperative VV ECMO was performed. ECMO support was discontinued on postoperative day 6. The patient was taken to a hospital on postoperative day 9. Oxygen administration at a rate of 2 L/min was required during the follow-up period. Acute graft rejection and infection were ruled out. Right diaphragm elevation was detected, so diaphragm plication was performed; mesenteric artery ischemia developed postoperatively. Colon and partial small bowel resection was performed due to ischemia. The patient died 45 days after lung transplantation.

One-year survival was achieved in 4 patients, whereas 1 died due to sepsis in the 4th month. In this patient with IIP, single lung transplantation was performed on the 55th day of VV ECMO due to intensive intraoperative bleeding. In the 4th month of follow-up, the lesion was radiologically compatible with aspergillosis, and bronchoscopic specimen culture showed Aspergillus spp. growth in the donor lung. In the patient with acute deterioration, bronchoalveolar lavage culture identified Pseudomonas aeruginosa, and the patient died of sepsis. The patient was incidentally diagnosed with mixed-type adenoma and died due to brain metastasis in the 13th month. There was no radiological relapse in the patient with transplanted lung (Table 3).

**Discussion**

Among patients on the waiting list for lung transplantation, mortality rate is high due to the small number of suitable donors and the rapid deterioration of patient condition. These patients generally require mechanical ventilatory support in ICUs. High-pressure, high FIO2 support is required for this mechanical ventilation. Ventilatory support increases the risk of microbial airway colonization and leads to loss of respiratory muscle strength. Moreover, prolonged ventilation may result in pneumonia. Owing to ventilator-related complications in cases with prolonged mechanical ventilatory support, the use of ECMO as a bridge to lung transplantation can be considered a relative contraindication (3).

However, the use of ECMO as a bridge to lung transplantation ensures that patients remain suitable candidates for such transplantation. Owing to the lack of donor organs, it can be considered that lung transplantation is not appropriate in patients with severe respiratory and hemodynamic decompensation. Although bridging strategies for lung transplantation increases the risk of major complications, hospital mortality and cost, the recent achievement of good results following the use of ECMO as a bridge to lung transplantation, particularly the awake strategy, has encouraged their co-use (10). A report published by the United Organ Sharing Network showed that the use of ECMO as a bridge to lung transplantation has increased by 150% between 2010 and 2012 compared with its use before 2010 (11). Moreover, in a study by Typograf et al. involving 70 patients, the 1-year survival rate was 88% upon successful bridging to lung transplantation and 87% in all transplant recipients (12). Likewise, many studies have reported no difference in the long-term survival of patients between those with and without ECMO bridging in lung transplantation (6, 8, 9, 13, 15). However, the use of ECMO as a bridge to lung transplantation is associated with increased primary graft dysfunction and prolonged hospitalization. The need for blood transfusion increases with the development of systemic inflammatory response in addition to coagulopathy with the prolongation of ECMO time. Therefore, the risk of primary graft dysfunction increases. High-volume transplant clinics (with > 50 transplants annually) are more likely to cope with these problems due to the more aggressive use of postoperative ECMO (4–6). The use of ECMO during the early period of primary graft dysfunction is a potential treatment option to save donor lungs with acceptable survival and complication rates (16).

The use of ECMO as a bridge to lung transplantation is contraindicated in the presence of a neurological deficit, multidrug-resistant infection, and multiorgan failure. Although the presence of bacteremia is not a contraindication, transplantation should not be performed without treating the infection. One of our patients died of sepsis due to bacteremia, despite an uneventful operation and early intensive care. Patients receiving ECMO are indisputably at high risk of developing nosocomial infection,
with 6.1% of neonates and 20.5% of adults acquiring a culture-proven infection during ECMO (17). Currently, the Extracorporeal Life Support Organization Infections Disease Task Force does not recommend routine antimicrobial prophylaxis during ECMO, although, to date, no systematic reviews of prophylaxis in ECMO have been performed. Practice has varied from multidrug therapy for the entire run of ECMO to selective gram-positive coverage and to the absence of antibiotic use beyond surgical prophylaxis for cannulation. Based on the consensus of infectious disease experts and the subsequent conclusion and recommendation of the task force that there are no data to support the routine use of continued antibiotics for patients on ECMO support, solely for prophylaxis without specific culture or physiological evidence of ongoing infection, it has been reported that the common practice of continuous administration of prophylactic antibiotics may likely only increase the risk of infection with resistant strains and that of potential yeast overgrowth (18). However, the recommendation of avoiding the routine use of antibiotic prophylaxis for patients on extracorporeal support does not necessarily apply to cardiothoracic patients with transthoracic cannulation via open chest, a group of patients with a documented increased risk of infection, specifically mediastinitis (19, 20). Because of the increased incidence of fungal infections in patients under ECMO support and high mortality observed among these patients, cautious but aggressive use of antifungal prophylaxis is particularly recommended for high-risk patients. At our center, in accordance with these recommendations, all infection prevention precautions are implemented on the basis of prior or current microbiological status for both patients with ECMO as a bridge to lung transplantation and those with the other indications of ECMO. Antibiotic use in this group is based on the clinical judgment of the team and multiple factors including the duration of open chest, overall immune and nutritional status, previously known colonization with multidrug-resistant microorganisms, and the perceived risk of contamination of the open wound. Weekly screening cultures from different sites are taken for early prevention and initiation of antibiotic therapy when necessary. If a patient has been previously colonized or infected before ECMO cannulation, we empirically use antipseudomonal beta-lactams, glycopeptides, or their combination according to the history of causative agents of infection in the patient. If the patient is being maintained on open chest, we routinely use echinocandins for 14 days.

The risk of bleeding requiring surgical intervention after lung transplantation was reported to be 12.6–15% (21,22). This risk increases in the presence of preoperative ECMO. The major intraoperative problem was severe bleeding due to pleural adhesions. Massive blood transfusions can have serious side effects that may be life-threatening. They may lead to decreased platelet count and concentration of coagulation factors. Bleeding becomes more marked in cases of infection, shock, and disseminated intravascular coagulation. Replacing coagulation factors and platelets helps control bleeding. Platelet suspension should be considered if the platelet count is < 50,000/μl or < 100,000/μl and continues to drop rapidly.

During the preoperative period, one of the major problems is the requirement of erythrocyte suspension. We have frequently encountered hemolysis in these patients due to the high flow rate of ECMO. When delivering oxygen to patients receiving ECMO, low flow is required because the hemoglobin value increases. Our targeted hemoglobin level was 12 mg/dl, but it could not be achieved in the initial days of ECMO administration. We found that as patients were supported by erythrocyte suspension, their physiological needs were met. This reduced the need for mechanical ventilatory support in addition to ECMO. We used erythrocyte suspension for the success of ECMO bridging despite the risk of future antibody formation. Leukocyte-depleted packed RBCs were used for transfusion.

All patients receiving ECMO should receive physiotherapy including those who cannot be taken off mechanical ventilator. Femoral cannulation does not interfere with the physical activities of the patient. As far as possible, “awake” ECMO strategies should be used (10–23). Awake VV ECMO is used to prevent sedation and invasive mechanical ventilatory support to protect respiratory muscles and facilitate active mobilization (24). In addition to early mobilization, normal eating and drinking are important for coping with psychological and physiological problems. In the majority of patients, VV ECMO is sufficient to meet physiological needs. However, in the presence of severe pulmonary hypertension, patient condition may deteriorate due to right heart failure. In such cases, conversion to VA ECMO can be performed or, even from the beginning, VA ECMO should be considered. Right heart failure during ECMO administration and positive fluid balance during follow-up indicate poor prognosis of successful bridging. Ideal patients are those who are young and on the waiting list for lung transplant. We successfully bridged 3 of the 4 patients on our waiting list. One-year survival was achieved in 2 patients, and they are being continually followed up.

More data are needed to support the optimal time for applying ECMO. It should be used not only to provide respiratory invasive support but also to provide physiological support. It may enable the prevention of cardiac arrest due to sudden deterioration of condition. The duration of ECMO support is the most common factor potentially affecting post-transplant mortality and morbidity. Crotti et al. divided patients into two groups in terms of the ECMO support period using a threshold of 14 days. The patients were observed to have worse mortality and survival if the period.
 lasted for > 14 days (25). Moreover, in a study by Inci et al., the median waiting period was 21 days; remarkably, better survival was observed in patients with a waiting period of > 14 days (26). Patients receiving ECMO as a bridge to lung transplantation should be routinely reassessed to ensure that they do not meet any exclusion criterion for lung transplantation, to ensure optimal benefits, and to avoid futile transplantations.

Limitations

The present study has several limitations. Our study was retrospective, and it is ethically impossible to perform a prospective study on this issue. In addition, we did not include patients who were receiving ECMO but who were not included in the waiting list. The condition of these patients did not allow transplantation at an external center. Moreover, owing to the limited experience of patients bridged to lung transplant via mechanical support in Turkey, our sample size is limited. We also did not compare our study patients with those not receiving ECMO. Furthermore, the median waiting period for transplant was only 4 months in all patients. During the study period, we performed 55 lung transplants and lost 34 patients on the waiting list. We believe that such a comparison would be misleading because most of our patients were borderline cases for ECMO support. In the use of ECMO as a bridge to lung transplantation, the ventilation strategy applied to patients was not defined (in terms of positive end-expiratory pressure, tidal volume, and inspiratory pressure). The ventilation strategy varied daily according to patient conditions and the efficiency of the ECMO oxygenator. In almost all patients, the native lung did not participate in the oxygenation. ECMO support had to be provided with a full flow rate. Furthermore, mechanical ventilatory support was avoided whenever possible. Based on our limited experience, we prefer the use of ECMO as a bridge to lung transplantation, but we avoid using it in patients in a very poor condition. We do not consider it ethical to refuse bridging with ECMO, particularly in young patients.

Conclusion

Patients awaiting lung transplant are at high risk of mortality. The use of ECMO as a bridge to lung transplantation in the modern era of lung transplantation has become more acceptable with the excellent results reported in recent literature regarding patients in rapid decline. However, appropriate patient selection such as those on the waiting list for lung transplantation, young patients, and well-rehabilitated patients, is important to achieve optimal benefits.

Compliance with ethical standards

Conflict of interest None declared.

References

1. Roux A, Beaumont-Azuar L, Hamid AM, De Miranda S, Grenet D, Briend G, Bonnette P, Puyo P, Parquin F, Devaquet J, Trebbia G, Cuquemelle E, Douvry B, Picard C, LeGuen M, Chapelier A, Stern M, Sage E; FOCH Lung Transplant Group. High emergency lung transplantation: dramatic decrease of waiting list death rate without relevant higher post-transplant mortality. Transpl Int. 2015;28:1092–101.
2. Beitler JR, Malhotra A, Thompson BT. Ventilator-induced lung injury. Clin Chest Med. 2016;37:633–46.
3. Singer JP, Blanc PD, Hoopes C, Golden JA, Koff JL, Leard LE, Cheng S, Chen H. The impact of pretransplant mechanical ventilation on short- and long-term survival after lung transplantation. Am J Transplant. 2011;11:2197–204.
4. Mason DP, Thuita L, Novicki ER, Murthy SC, Pettersson GB, Blackstone EH. Should lung transplantation be performed for patients on mechanical respiratory support? The US experience. J Thorac Cardiovasc Surg. 2010;139:765–73.
5. Chiumello D, Coppola S, Froio S, Colombo A, Del Sorbo L. Extracorporeal lifesupport as bridge to lung transplantation: a systematic review. Crit Care. 2015;22(19):19.
6. Hayanga AJ, Aboagye J, Harper S, Shigemura N, Bermudez CA, D’Cunha J, Bhama JK. Extracorporeal membrane oxygenation as a bridge to lung transplantation in the United States: an evolving strategy in the management rapidly advancing pulmonary disease. J Thorac Cardiovasc Surg. 2015;149:291–6.
7. Weill D, Benden C, Corris PA, Dark JH, Davis RD, Keshevee S, Lederer DJ, Mulligan MJ, Patterson GA, Singer LG, Snell GI, Verleden GM, Zamora MR, Glanville AR. 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. Toyoda Y, Bhama JK, Shigemura N, Zaldonis D, Pilewski J, Crespo M, et al. Efficacy of extracorporeal membrane oxygenation as a bridge to lung transplantation. J Thorac Cardiovasc Surg. 2013;145:1065–71.
9. Hoopes CW, Kukreja J, Golden J, Davenport DL, Diaz-Guzman E, Zwischenberger JB. Extracorporeal membrane oxygenation as a bridge to pulmonary transplantation. J Thorac Cardiovasc Surg. 2013;145:862–8.
10. Fuehner T, Kuehn C, Hadem J, Wiesner O, Gottlieb J, Tudorache I, et al. Extracorporeal membrane oxygenation in awake patients as a bridge to transplantation. Am J Respir Crit Care Med. 2012;185:763–8.
11. Diaz-Guzman E, Hoopes CW, Zwischenberger JB. The evolution of extracorporeal life support as a bridge to lung transplantation. ASAIO J. 2013;59:3–10.
12. Tipograf Y, Salma M, Minko E, Grogan EL, Agerstrand C, Sonett J, Brodie D, Bacchetta M. Outcomes of extracorporeal membrane oxygenation as a bridge to lung transplantation. Ann Thorac Surg. 2019;107:1456–63.
13. Langer F, Aliev P, Schaefers HJ, et al. Improving outcomes in bridge-to-transplant: extended extracorporeal membrane oxygenation support to obtain optimal donor lungs for marginal recipients. ASAIO J. 2018;106:1812–9.
14. Schechter MA, Ganapathi AM, Englum BR, Speicher PJ, Daneshmand MA, Davis RD, et al. Spontaneously breathing extracorporeal membrane oxygenation support provides the optimal bridge to lung transplantation. Transplantation. 2016;100:2699–704.

15. Javidfar J, Brodie D, Iribarne A, Jurado J, Lavelle M, Brenner K, Arcasoy S, Sonett J, Bacchetta M. Extracorporeal membrane oxygenation as a bridge to lung transplantation and recovery. J Thorac Cardiovasc Surg. 2012;144:716–21.

16. Bermudez, Adusumilli PS, McCurry KR et al. Extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation: long term survival. Ann Thorac Surg 2009;87:554–60.

17. Bizzarro MJ, Conrad SA, Kaufman DA, Rycus P. Extracorporeal life support organization task force on infections, extracorporeal membrane oxygenation: infections acquired during extracorporeal membrane oxygenation in neonates, children, and adults. Pediatr Crit Care Med. 2011;12:277–81.

18. Extracorporeal Life Support Organization. ECLS Registry Report International Summary. January 2019. https://www.elso.org/. Accessed 7 Feb 2019.

19. O’Neill JM, Schutze GE, Heulitt MJ, Simpson PM, Taylor BJ. Nosocomial infections during extracorporeal membrane oxygenation. Intensive Care Med. 2001;27:1247–53.

20. Coffin SE, Bell LM, Manning ML, Polin R. Nosocomial infections in neonates receiving extracorporeal membrane oxygenation. Infect Control Hosp Epidemiol. 1997;18:93–6.

21. Hong A, King CS, Brown AW, Ahmad S, Shlobin OA, Khandhar S, Bogar L, Rongione A, Nathan SD. Hemothorax following lung transplantation: incidence, risk factors, and effect on morbidity and mortality. Multidiscip Respir Med. 2016;11:40.

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.