Extracorporeal membrane oxygenation as a bridge to lung transplantation and recovery

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Objective: Respiratory failure develops in many patients on lung transplant waiting lists before a suitable donor organ becomes available. Extracorporeal membrane oxygenation may be used to bridge such patients to recovery or lung transplantation.

Methods: This is a review of a single-institution's experience with placing patients on extracorporeal membrane oxygenation with the intention of bridging them to lung transplantation. End points included successful bridging, duration of extracorporeal membrane oxygenation support, extubation, weaning from extracorporeal membrane oxygenation, overall survival, and extracorporeal membrane oxygenation–related complications. During an approximate 5-year period, acute respiratory failure developed in 18 patients (median age, 34 years) on the institution's lung transplant waiting list (8 hypoxemic, 9 hypercarbic, and 1 combined) who were placed on extracorporeal membrane oxygenation (13 venovenous and 5 venoarterial).

Results: All patients achieved appropriate extracorporeal membrane oxygenation blood flow rates (median, 4.05 L/min) and good gas exchange (median, on extracorporeal membrane oxygenation partial pressure of arterial carbon dioxide 43 mm Hg and partial pressure of arterial oxygen 196 mm Hg). Thirteen patients (72%) were successfully bridged: 10 to transplant and 3 returned to baseline function. Eleven patients (61%) survived beyond 3 months, including the 10 (56%) who underwent transplantation and are still alive. The median duration of extracorporeal membrane oxygenation support for patients who underwent transplantation was 6 days (3.5-31 days) versus 13.5 days (11-19 days) for those who did not undergo transplantation ($P = .45$). Six patients (33%) were extubated on extracorporeal membrane oxygenation, 4 of whom underwent transplantation. Four patients (22%) who were too unstable for conventional interhospital transfer were transported on extracorporeal membrane oxygenation to Columbia University Medical Center. This subgroup had a 75% bridge to transplant or recovery rate and 100% survival in transplanted patients.

Conclusions: Extracorporeal membrane oxygenation is a safe and effective means of bridging well-selected patients with refractory respiratory failure to lung transplantation or return to their baseline condition. (J Thorac Cardiovasc Surg 2012;144:716-21)

Given the 12- to 24-month waiting period, patients with end-stage lung disease can acutely decompensate and develop refractory respiratory failure before suitable donor lungs become available.[1] The need for prolonged invasive mechanical ventilation may render these patients unsuitable for transplantation.

Patients with respiratory failure requiring mechanical ventilation can be temporarily supported on extracorporeal membrane oxygenation (ECMO) while they wait for a lung transplant if mechanical ventilation alone is insufficient to meet their gas exchange needs.[2,3] ECMO may even allow some patients to be removed from mechanical ventilation while they await transplantation, which permits patients to eat, to participate in their own care, and to work more extensively with physical therapists, including ambulating with assistance. This has the potential to improve their pretransplant conditioning during this critical illness phase rather than allowing it to worsen, which is typically the case in these patients.

Venovenous ECMO is often sufficient to support such patients' physiologic needs. However, when there is significant pulmonary hypertension, an acute exacerbation can lead to right-sided heart failure that benefits from the ventricular unloading afforded by venoarterial ECMO.

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Abbreviations and Acronyms

ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
IQR = interquartile range
Pa_{O_2} = partial pressure of arterial oxygen
Pa_{CO_2} = partial pressure of arterial carbon dioxide

To date, the routine use of modern mechanical circulatory support to bridge patients to lung transplantation has been limited.[4] The paucity of experience in the literature has prevented any durable conclusions regarding the safety and efficacy of such a strategy. Most previous reports have been limited by the use of multiple extracorporeal life support techniques, outdated technology, and small sample size.[5,6]

We report on the use of contemporary ECMO technology and management strategies to bridge patients listed for lung transplantation who subsequently developed an acute exacerbation of their underlying respiratory failure requiring invasive mechanical ventilation.

PATIENTS AND METHODS

This study, which was approved by the Columbia University Medical Center Institutional Review Board, is a retrospective review of a single institution's experience with bridging patients on the active lung transplant list to transplantation or recovery using ECMO support.

Patient Selection

The decision to place patients on ECMO was made by a team composed of thoracic surgeons, critical care intensivists, and transplant pulmonologists. To be a bridge candidate, a patient needed to be on the institution's active lung transplant waiting list. The indications for considering ECMO support were the presence of hypoxemic or hypercarbic respiratory failure requiring invasive mechanical ventilation with high levels of support or worsening right-sided heart failure.[7] The lung diseases associated with hypoxemic respiratory failure included exacerbation of interstitial pulmonary fibrosis and pulmonary hypertensive crisis due to a congenital heart defect. In these patients, a partial pressure of arterial oxygen tension (Pa_{O_2}) to inspired oxygen fraction less than 80 was needed before initiation of ECMO. Hypercarbic respiratory failure (uncompensated hypercapnia with acidosis, pH < 7.25 despite optimal ventilator management) was seen in patients with an exacerbation of cystic fibrosis.

Patients who acquired a known contraindication to continuing ECMO support were decannulated. If a suitable donor lung was immediately available, patients were considered for transplant. Otherwise, the patient was delisted if temporarily maintaining the patient with mechanical ventilation alone was not feasible. Criteria for delisting a patient, whether temporarily or permanently, were consistent with institutional and United Network for Organ Sharing guidelines for all patients on the lung transplant waiting list. This included delisting patients who contracted and could not resolve *Clostridium difficile* colitis or who developed multiorgan system dysfunction while on ECMO. The institutional lung transplant selection committee made listing decisions. The transplant pulmonologists and cardiothoracic surgeons used the institution's standardized donor lung evaluation protocol to evaluate donor lungs for patients on ECMO.

Protocol

The cannulation techniques used were specific to the ECMO configuration deemed by the ECMO team to best serve the patient's physiologic needs. Patients were placed on venovenous ECMO via the internal jugular vein or venoarterial ECMO via femoral or subclavian arteries using previously described techniques.[8,9] Patients with a congenital heart defect had the right internal jugular vein cannulated with a bicaval dual-lumen cannula under transesophageal echocardiographic guidance according to a previously described technique.[10] The cannulae were attached to a standardized circuit. The ECMO circuit consisted of a Quadrox D or Quadrox I oxygenator (Maquet Inc, Rastatt, Germany) and a Jostra Rotaflow (Maquet Inc) or Levitronix Centrimag (Levitronix, GmbH, Zurich, Switzerland) centrifugal pump.

If patients on Columbia University Medical Center's lung transplant list decompensated at an outside hospital and were thought to be appropriate bridge to transplant candidates, they were cannulated at the outside hospital and transported via a mobile ECMO unit per standardized protocol.[11] All patients were managed on ECMO according to a low-dose anticoagulation protocol (a partial thromboplastin time of 40-60 seconds). There was a high threshold for blood product transfusion with the goal of minimizing the creation of future antibodies, especially if a delay in transplantation was expected.[12,13] Leukocyte-depleted packed red blood cells were used for transfusion. Patients did not receive a transfusion unless it was needed to meet physiologic demand.

A review of the clinical records was conducted to obtain information regarding the patient's pre-ECMO status, operative course, hospitalization, and intensive care unit (ICU) stay. End points included successful bridging, duration of ECMO support, extubation, weaning from ECMO, overall survival, and ECMO-related complications.

Statistical Methods

All statistical analyses were performed with a statistical package (Stata 11; StataCorp LP, College Station, Tex). The total median ICU stay consisted of pre-ECMO, on-ECMO, and post-transplant ICU stays. Median values were provided with interquartile ranges (IQRs). To minimize potential concerns regarding normality of the data distribution, nonparametric rank-sum tests were used to compare continuous variables where appropriate. Categoric variables were compared using chi-square tests. The Wilcoxon Mann–Whitney rank-sum test, Fisher exact test, and univariate logistic regression were used for comparisons and subgroup analysis. A successful bridge was defined as any patient on the lung transplant waiting list who underwent transplantation or recovered after being placed on ECMO. Survival comparisons were made with Kaplan–Meier analysis, with survival estimates compared using a log-rank test. Overall survival was defined as the time from placement on ECMO to death or last follow-up through April 15, 2012. For the purpose of assessing statistical significance, a conventional alpha of 0.05 was used.

Demographics

From July 2007 to April 2012, 18 patients on the lung transplant list who experienced acute respiratory failure requiring invasive mechanical ventilation were placed on ECMO as a bridge to transplantation. This represents less than 10% of the total patients placed on ECMO during this period and is the entire institutional experience with bridging patients to lung transplantation using ECMO.

Nine patients experienced hypercarbic respiratory failure with a median pre-ECMO pH of 7.17 and median partial pressure of carbon dioxide of 123 mm Hg. One patient had combined hypercarbic and hypoxemic respiratory failure. The remaining 8 patients had hypoxemic respiratory failure with Pa_{O_2} to fraction of inspired oxygen of 63 (Table 1). The patients with pulmonary hypertensive crises had systemic or suprasystemic pulmonary artery pressures and right ventricular failure confirmed on transthoracic or transesophageal echocardiography.

The majority of patients (72%) were supported for the entire extracorporeal life support course on venovenous ECMO. Five patients required venoarterial ECMO support. One patient was placed on femoral venoarterial