Efficacy of extracorporeal membrane oxygenation as a bridge to lung transplantation

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Background: Preoperative extracorporeal membrane oxygenation (ECMO) is a risk factor for poor outcome and currently considered a contraindication to lung transplantation. The lung allocation score system was introduced in May 2005 and prioritizes lung allocation to those with the greatest respiratory impairment. The purpose of this study is to determine whether ECMO as a bridge to lung transplantation is an acceptable option to support those in respiratory failure until donor lungs become available in the lung allocation score era.

Method: A retrospective review of 715 consecutive lung transplants performed between May 2005 and September 2011 was conducted using a prospectively collected institutional registry database. Twenty-four lung transplants (3.4%) were performed in the 31 patients with attempted pretransplant ECMO; 7 patients who received ECMO patients did not survive or were deemed unfit for transplantation. These patients were compared with a control group of 691 patients who did not receive pretransplant ECMO.

Results: The duration of pretransplant ECMO was 171 ± 242 hours (median, 91 hours). Venovenous ECMO was used for respiratory failure in 15 patients, whereas venoarterial ECMO was used for circulatory collapse due to pulmonary hypertension in 9 patients. Patients in the retransplant ECMO group were younger (46 ± 15 years vs 57 ± 14 years, $P < .01$) compared with the control group, with no difference in recipient gender (male/female: 10/14 vs 380/311), donor age (33 ± 14 years vs 36 ± 15 years), or donor gender (male/female: 10/14 vs 352/339). Emphysema was less common (1, 4% vs 260, 38%, $P < .01$), and cystic fibrosis (5, 21% vs 72, 10%, $P = .09$), redo lung transplant (3, 13% vs 28, 4%, $P = .08$), and bronchiectasis (2, 8% vs 6, 1%, $P = .03$) were more common in the pretransplant ECMO group. Patients in the pretransplant ECMO group had a significantly higher lung allocation score (87 ± 9 vs 44 ± 15, $P < .01$). All patients in the pretransplant ECMO group underwent double lung transplants on pump (cardiopulmonary bypass/ECMO), and single lung transplants were performed in 171 patients (25%) and pump was used in 243 patients (35%) in the control group. The cardiopulmonary bypass time was longer in the pretransplant ECMO group (277 ± 69 minutes vs 225 ± 89 minutes, $P = .02$), with no difference in ischemic time (343 ± 93 minutes vs 330 ± 98 minutes, $P = .54$). Cadaveric lobar lung transplants were performed because of the urgency to overcome size mismatch with an oversized donor more frequently in 25% (n = 6, no mortality with the longest follow-up at 6 years) of patients in the pretransplant ECMO group versus 0.3% (n = 2) of patients in the control group ($P < .01$). Post-transplant ECMO was used for primary graft dysfunction in 13 patients (54%) in the pretransplant ECMO group and 41 patients (6%) in the control group ($P < .01$). The median hospital stay was 46 days in the pretransplant ECMO group versus 27 days in the control group ($P = .16$). The actuarial survivals after lung transplants at 1, 3, 6, 12, and 24 months were 96%, 88%, 83%, 74%, and 74%, respectively, in the pretransplant ECMO group, and 97%, 94%, 90%, 83%, and 74%, respectively, in the control group ($P = .787$).

Conclusions: Although the incidence of primary graft dysfunction requiring post-transplant ECMO is higher and the hospital stay is longer in patients receiving pretransplant ECMO, the graft survival is good (2-year survival, 74%). ECMO is efficacious as a bridge to lung transplantation with good post-lung transplant outcomes. (J Thorac Cardiovasc Surg 2013;145:1065-71)

Extracorporeal membrane oxygenation (ECMO) has been used in clinical medicine for 40 years, but it remains a controversial therapy.[1] ECMO has been used as a life-support tool for critically ill patients who can no longer survive with optimum medical therapy, including maximal mechanical ventilator support, inhaled nitric oxide, and medications such as inotropes. Preoperative mechanical ventilation and hospitalization have been repeatedly shown

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Abbreviations and Acronyms
ECMO = extracorporeal membrane oxygenation
LAS = lung allocation score
UNOS = United Network for Organ Sharing
VA = venoarterial
VV = venovenous

to be significant risk factors for mortality in lung transplantation.[2] Because patients receiving ECMO are hospitalized and almost always on mechanical ventilation, it has been controversial whether patients on ECMO should receive lung transplantation, and in reality, these patients have been frequently denied for listing or removed from the waitlist, resulting in pretransplant mortality. Mason and colleagues[3] analyzed United Network for Organ Sharing (UNOS) data from 1987 to 2008 and found that only 51 patients (0.3%) in the United States were on ECMO preoperatively. The 1- and 2-year survivals were 50% and 45%, respectively, for patients with pretransplant ECMO compared with 79% and 70%, respectively, for unsupported patients. Therefore, ECMO has been considered a contraindication for lung transplantation in many centers because of the poor outcomes.

Before the introduction of the current lung allocation score (LAS) system in the United States in May 2005,[4] lung allocation was primarily based on waiting time. The waiting time–based lung allocation favors patients well enough to wait the longest and does not favor critically ill patients who cannot wait for a prolonged period of time.[5] Therefore, patients on ECMO might have to wait for a long time, and the outcomes of lung transplantation would be suboptimal because complications such as muscular deconditioning, infection, thromboembolism, bleeding, and poor nutrition could occur while waiting on ECMO. However, with the LAS system, critically ill patients who are in imminent danger of death and therefore in direst need of lung transplantation receive a high score and have priority of lung allocation.[4,5] Patients on ECMO have a high LAS,[3] possibly resulting in finding suitable donor lungs in a timely fashion, and therefore potentially leading to better outcomes.

We have recently reported our experience of pretransplant ECMO.[6] However, the study included both lung and heart-lung transplant recipients and patients who were under various protocols from 1991 to 2010. In addition to the change in the lung allocation in 2005, we have made several important changes in our protocols, including preservation solution of the donor lungs, intraoperative pulmonary protection, postoperative ventilator management, and immunosuppression from 1991 to 2003.[7,8] Therefore, the purpose of this study was to review the efficacy of ECMO as a bridge to lung transplantation, not including heart-lung transplantation, following the instrumentation of the current LAS system in 2005 in our current, standardized protocols at a single institution.

PATIENTS AND METHODS

Study Protocol

The University of Pittsburgh Medical Center lung transplant evaluation and recipient research registry is approved by the University of Pittsburgh Institutional Review Board for the use of patient management, quality assurance reports, and clinical research. Data were prospectively collected into the Transplant Patient Management System. We performed a retrospective analysis of consecutive patients, from May 2005 to September 2011, who underwent lung transplant (primary and retransplantation). Data were obtained from the University of Pittsburgh Medical Center transplant database and patient charts. This study was approved by the Total Quality Council at the University of Pittsburgh Medical Center. The informed consent requirement was waived.

Patient Selection

ECMO was selectively used to support patients with advanced cardiopulmonary failure unresponsive to maximal medical therapy, such as mechanical ventilation support with 100% inspired oxygen fraction, positive end-expiratory pressure, and use of inhaled nitric oxide and inotropes. ECMO was considered for patients who presented a rapid deterioration of a chronic lung disease while on the waiting list or during the lung transplant evaluation process. Three patients on ECMO support for primary graft failure after the primary lung transplant with the absence of lung recovery were selectively considered for redo lung transplantation. We considered retransplantation in the context of primary graft dysfunction when other organ functions were intact. We excluded patients who did not meet standard criteria for lung transplant candidacy. Therefore, patients with other established organ dysfunctions, including renal failure, liver failure, major stroke, and sepsis, were denied. Patients who underwent lung transplantation without the use of pretransplant ECMO during the period analyzed served as a control group.

Lung Transplant Protocols

During the study period 2005 to 2011, standardized protocols were applied, which have been described.[7,8] In summary, for donor lung procurement, a bolus injection of prostaglandin E_1 500 μg was administered into the main pulmonary artery immediately before crossclamp. An additional 500 μg of prostaglandin E_1 and 50 mg of nitroglycerin were added in the first bag of Perfadex (Vitrolife AB, Gothenburg, Germany). We administered 70 mL/kg of Perfadex antegradely through the main pulmonary artery in the operative field and 1 liter of Perfadex for each lung retrogradely through the pulmonary veins at the back table. During the recipient surgery, 800 mL of cold blood with glutamate, aspartate, lidocaine, adenosine, nitroglycerin, verapamil, deferoxamine, ascorbic acid, dextrose, and insulin, as described previously,[7] were given antegradely through the pulmonary artery after the bronchial anastomosis, and 800 mL of terminal warm blood with the same additives were given antegradely through the pulmonary artery before reperfusion to protect the allograft. Protective ventilatory management with low tidal volume (6 mL/kg of the donor body weight) and high positive end-expiratory pressure was used postoperatively. For immunosuppression, our standard immunosuppressive induction became alemtuzumab (Campath 1-H; Genzyme Corporation, Cambridge, Mass) in 2003, which was given intraoperatively. For maintenance immunosuppression, a triple drug regimen including tacrolimus, mycophenolate mofetil in half dose (750 mg twice daily), and minimized steroid (5 mg once daily) were used. For infection prophylaxis, valganciclovir was used for cytomegalovirus and voriconazole was used for fungus and yeast.