Outcome of Extracorporeal Membrane Oxygenation as a Bridge to Lung Transplantation and Graft Recovery

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Background. **Indications for extracorporeal membrane oxygenation (ECMO) use in lung transplantation are (1) temporary assistance as a bridge to transplantation, (2) stabilization of hemodynamics during transplantation in place of cardiopulmonary bypass, and (3) treatment of severe lung dysfunction and primary graft failure after transplantation. This study compares the survival of lung transplant recipients requiring ECMO support with survival of patients without ECMO.**

Methods. **A retrospective database review was performed for 108 consecutive patients who underwent single-lung or bilateral-lung transplantation at our center between 2002 and 2009.**

Results. **Of 108 transplant recipients, 27 (25%) required venoarterial ECMO compared with 81 patients who did not. Nine patients required ECMO preoperatively (87 ± 102 hours), and ECMO was continued for 5 patients during the lung transplant operation. Seven additional patients received ECMO during transplantation. Six patients required early (< 7 days) and 5 patients delayed (≥7 days) postoperative ECMO for treatment of allograft dysfunction. The subgroup with support showed the most favorable patient discharge rate (66.7%). ECMO support was a significant risk factor for death ($p < 0.001$). Survival was significantly reduced with the use of ECMO: 30-day, 90-day, 1-year, and 5-year survival was 97%, 91%, 83%, and 58% in the patients without ECMO compared with 63%, 44%, 33%, and 21% in those with ECMO, respectively.**

Conclusions. **Survival after lung transplantation was significantly reduced with ECMO. However, patients who survived the first year showed similar long-term survival as those patients who did not need perioperative ECMO support.**

(Ann Thorac Surg 2012;94:942–50)

Lung transplantation (LTx) has become the standard of care for most causes of end-stage lung disease [1] and can be achieved with low operative mortality rates. However, outcome is affected by the shortage of donor organs, leading to increased waiting list times with deteriorating patient conditions and a relatively high rate of primary graft dysfunction [2]. Extracorporeal membrane oxygenation (ECMO) is increasingly used as rescue therapy for primary graft dysfunction after LTx [3–5]. Several groups recently reported the successful use of ECMO as a bridge-to-transplantation in patients who were unresponsive to maximal pulmonary-respiratory support [6–8]. ECMO can also be used as an alternative technique of extracorporeal circulation for oxygenation and hemodynamic support during LTx in place of cardiopulmonary bypass [9]. Owing to refinements in surgical technique, including central and peripheral ECMO implantation techniques, ECMO support can be applied to the individual patient situation.

Modern ECMO technology uses oxygenators with reduced blood cell contact surface area and heparin-bonded circuits. ECMO now has the capacity to support gas exchange and hemodynamics without the need for high-dose heparin administration and anticoagulation therapy. The broadened indications for ECMO have increased its application in LTx; however, only limited data are available to compare patient outcomes with the use of ECMO before, during, and after the operative with the outcomes of patients who do not receive ECMO support [6]. Therefore, a case-control study was conducted to compare survival in LTx patients with and without venoarterial ECMO support.

Patients and Methods

The Ethics Committee at the University of Leipzig approved this study. Patients provided written informed consent for data registration and analysis at institutional, national, and international data registries (German Transplant Procurement Agency, Eurotransplant, and

Accepted for publication May 2, 2012.

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Presented at the Forty-eighth Annual Meeting of The Society of Thoracic Surgeons, Fort Lauderdale, FL, Jan 28–Feb 1, 2012.

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0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2012.05.006

Abbreviations and Acronyms

ARDS = acute respiratory distress syndrome
COPD = chronic obstructive pulmonary disease
CPB = cardiopulmonary bypass
ECMO = extracorporeal membrane oxygenation
FFP = fresh frozen plasma
LTx = lung transplantation
MOF = multiorgan failure
OR = odds ratio
PAP = pulmonary arterial pressure
PRBC = packed red blood cells

the Registry of the International Society for Heart and Lung Transplantation).

Study Design

We performed a single-center database analysis of the prospectively collected data of our LTx recipients to determine the effect of ECMO support on outcome. Collected follow-up data included laboratory values, pulmonary function test results, bronchoscopy results, survival status, and cause of death.

Patient Population

From November 2002 (first LTx at our cardiothoracic unit) through December 2009, 108 patients (63% men) underwent LTx. Recipients were a mean age of 51.4 ± 11 years. Of these, 58 patients (54%) underwent single LTx and 50 had sequential bilateral LTx for various end-stage lung diseases. Indications for LTx were restrictive pulmonary disorders in 53%, chronic obstructive lung disease in 34%, cystic fibrosis in 7%, and primary pulmonary hypertension in 6%. Invasive pulmonary artery pressure monitoring revealed systolic pulmonary artery pressures exceeded 60 mm Hg in 70% of the recipients.

Six patients had also heart operations, such as aortic, tricuspid, or mitral valve interventions, as well as congenital heart defect repair or coronary artery bypass grafting. The analysis excluded data for 3 patients with combined heart-lung transplantation.

The standard recipient immunosuppressive protocol was a triple-medication regimen consisting of oral glucocorticoids, tacrolimus, and mycophenolate mofetil [10].

Surgical Procedures and Cannulation Techniques

We used well-established criteria for accepting donor lungs, including objective evidence of adequate gas exchange and bronchoscopic evaluation to exclude aspiration or purulent secretions [11]. Standardized organ procurement and recipient implantation techniques were used for LTx [12]. Whenever possible, anterior sternum-sparing and internal mammary artery-sparing thoracotomy incisions were used for single or bilateral sequential LTx [13]. The standard approach for ECMO was through a peripheral access (axillary or femoral artery and vein) to obtain an unobstructed exposure of the right lung hilum and an undisturbed surgical field.

After the cutdown of the femoral or right axillary artery, monofilament 5-0 purse-string sutures were applied to the anterior wall of the axillary or femoral artery and vein. The Seldinger cannulation technique was used to introduce the heparin-bonded venous (usually 22F) and arterial cannulas (18F). Transesophageal echocardiography was applied to control the positioning of guidewire and venous cannula within the right atrium.

To avoid limb ischemia and access-site complications with peripheral cannulation, we optimized the distal limb perfusion by using an 8-mm Dacron (DuPont, Wilmington, DE) T-graft (end-to-side anastomosis to the femoral or axillary artery), which was passed through a separate skin stab wound. The arterial cannula was passed through the Dacron graft until the tip of the cannula reached the anastomosis and pointed to the proximal site of the artery.

ECMO Support

The 108 patients underwent 50 bilateral sequential and 58 single LTxs. Idiopathic pulmonary fibrosis was the main reason for LTx in 49, followed by chronic obstructive pulmonary disease in 35 patients.

ECMO support was required in 27 LTx recipients: 9 preoperatively, 7 intraoperatively and 11 postoperatively. ECMO support was needed in 6 of these patients in the first 7 days ("early" support) postoperatively and was instituted in 5 patients after 7 days postoperatively ("late" support). A retrospective review of prospectively collected data on the 27 patients who received ECMO after LTx forms the basis of this review.

ECMO Support Devices and Management

The ECMO circuits consisted of the Medtronic Carmeda heparin-bonded tubing (Medtronic Cardiopulmonary, Anaheim, CA) and a centrifugal blood pump (Biomedicus Biopump, Medtronic, Minneapolis, MN) or the Levitronix (Centrimag, Pharos LLC, Waltham, MA) blood-pumping system for prolonged support, which propelled blood through a hollow-fiber membrane oxygenator (COBE, Cardiovascular, Anvada, CO, or Medos Medizintechnik AG, Stolberg, Germany), and since 2006, the Quadrox (Jostra Medizintechnik AG, Hirrlingen, Germany) hollow-fiber membrane oxygenator with integrated heat-exchanger. An oxygen/air blender (Sechrist Industries, Anaheim, CA) was used to ventilate the membrane oxygenator.

Blood flows were monitored by a Doppler flow probe placed on the arterial side of the circuit. Preoperative and postoperative ECMO flows were kept to 2.0 to 2.4 L/min/m^2. If ECMO was used intraoperatively as CPB, the blood flow was kept higher than 2.4 L/min/m^2 according to the hemodynamic situation.

To prevent bleeding complications in heparinized patients with CPB for LTx, followed by ECMO support due to a failing graft, heparin was completely antagonized by protamine administration. Aprotinin was routinely administered until 2007 using a modified Hammersmith protocol. More recently, aprotinin was replaced by tranexamic acid. Additional coagulation factors, platelets,