Outcomes of Intraoperative Venoarterial Extracorporeal Membrane Oxygenation Versus Cardiopulmonary Bypass During Lung Transplantation

Christian A. Bermudez, MD, Akira Shiose, MD, Stephen A. Esper, MD, Norihisa Shigemura, MD, PhD, Jonathan D'Cunha, MD, PhD, Jay K. Bhama, MD, Thomas J. Richards, PhD, Peter Arlia, CP, Maria M. Crespo, MD, and Joseph M. Pilewski, MD

Department of Cardiothoracic Surgery, Department of Anesthesiology, and Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

Background. **The intraoperative use of cardiopulmonary bypass (CPB) in lung transplantation has been associated with increased rates of pulmonary dysfunction and bleeding complications. More recently, extracorporeal membrane oxygenation (ECMO) has emerged as a valid alternative method of support and has been our preferred method of support since March 2012. We compared early and midterm outcomes of these 2 support methods.**

Methods. **Between July 2007 and April 2013, 271 consecutive patients underwent lung transplant using CPB (n = 222) or ECMO (n = 49). We retrospectively reviewed the outcomes of these patients requiring CPB or ECMO during lung transplant.**

Results. **The CPB and ECMO groups had comparable demographic and operative characteristics; however, the ECMO group had higher mean lung allocation scores (73 vs 52, $p < 0.001$). In the CPB group, more patients required reintubation (35.6% vs 20.4%, $p = 0.04$) or temporary tracheostomy (44.6% vs 28.6%, $p = 0.05$). Patients in the CPB group had a higher rate of renal failure requiring dialysis than the ECMO group (22.1% vs 8.2 %, $p = 0.028$). There were no differences in severe PGD requiring postoperative circulatory support ($p = 0.83$) or the need for perioperative red blood cell transfusions ($p = 0.64$) between the groups. No differences in 30-day (5% CPB vs 4.1% ECMO) or 6-month mortality (14.4% CPB vs 14.3% ECMO) were noted.**

Conclusions. **The use of ECMO in lung transplant is safe and in our experience was associated with decreased rates of pulmonary and renal complications, as compared with CPB. Extracorporeal membrane oxygenation has become our preferred method of intraoperative support during lung transplantation.**

(Ann Thorac Surg 2014;98:1936–43)

Lung transplantation (LT) is considered a valid therapeutic option in the treatment of advanced end-stage lung disease. Important advances have been made in the perioperative management of the patients undergoing LT with improved outcomes and acceptable rates of primary graft dysfunction (PGD) and postoperative complications. Although LT is frequently performed off-pump, circulatory support is necessary in 30% to 40% of patients who undergo LT [1]. Pulmonary support is most frequently necessary in recipients with significant pulmonary hypertension, right ventricular dysfunction, or who are unable to tolerate single-lung ventilation during LT, all frequent signs of advanced, end-stage lung disease.

Cardiopulmonary bypass (CPB) has been historically considered the standard method of intraoperative support during LT [1]. Although CPB provides adequate conditions to successfully complete a high-risk LT, CPB use significantly activates coagulation and inflammatory cascades and requires high-dose anticoagulation due to the number of blood-activating surfaces, including plastic tubing, a reservoir, and suction lines. For these reasons, CPB is associated with higher risk of bleeding, PGD, and other pulmonary complications as compared with LT performed without the use of CPB [2–4].

Extracorporeal membrane oxygenation (ECMO) uses a low-profile centrifugal pump and a membrane oxygenator in a closed, more limited circuit. ECMO was initially used in pediatric patients and in cases of profound acute lung injury. Improvements in the ECMO technology and experience gained more recently with ECMO use in patients with PGD (post-LT) [5] and with ECMO as a bridge to LT [6, 7] have stimulated ECMO use as a method of intraoperative support. Using ECMO for intraoperative circulatory support has the potential to decrease bleeding complications (due to lower heparin doses), PGD, and other complications associated with the activation of

Accepted for publication June 30, 2014.

Presented at the Fiftieth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Jan 25–29, 2014.

Address correspondence to Dr Bermudez, UPMC Presbyterian, Ste C-920, 200 Lothrop St, Pittsburgh, PA 15213; e-mail: bermudezc@upmc.edu.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.06.072

blood components and inflammation. Furthermore, intraoperative ECMO allows the continuation of support using the same system in cases of severe PGD. In this study we compared early outcomes of LT using these 2 methods of intraoperative support.

Patients and Methods

Study Protocol

We performed a retrospective analysis of patients requiring intraoperative mechanical support during LT. Between July 2007 and April 2013, 647 consecutive patients underwent primary LT in our institution. Of these, 374 patients (58%) were performed off-pump and 273 (42%) required the use of intraoperative mechanical support, including 222 patients who received CPB support, 49 patients who were supported with ECMO, and 2 patients requiring combined CPB and ECMO support. Consistent with current usage in the fields of pulmonary and circulatory support, we use the term ECMO to describe a limited bypass system utilizing an oxygenator and limited tubing that avoids the use of a reservoir with stagnant blood. Since March 2012, ECMO has been our preferred method of support with only 2 patients requiring CPB. These 2 patients began LT on ECMO, were switched to CPB due to uncontrolled bleeding, and were excluded from this study. Redo LTs (20 patients) during the same period were also excluded. Data were obtained from the University of Pittsburgh Medical Center transplant database and patients' charts. This study was approved by the Institutional Review Board and the informed consent requirement was waived.

Patients and Support Selection

Intraoperative mechanical support is routinely considered at our center in patients with severe pulmonary hypertension (transpulmonary pressure gradient $>$ 20 mm Hg), the inability to tolerate single-lung ventilation, hemodynamic derangement after pulmonary artery clamping, or who require associated cardiac procedures. More recently we have considered intraoperative mechanical support during lobar lung transplant to prevent hyperperfusion of the reduced size allograft.

Historically, we used CPB in all patients undergoing LT, necessitating intraoperative support. Beginning in 2008, as we observed an increasing number of patients supported preoperatively with ECMO before undergoing LT (ECMO bridge), we considered the continuation of the same support during the intraoperative procedure. Venoarterial (VA) ECMO was maintained during the LT surgery or venovenous (VV) ECMO was converted to VA ECMO to simplify the surgical approach, especially in cases when ECMO support was considered to be extended postoperatively. Since March 2012, ECMO has become our preferred method of support and we utilize CPB only in patients needing combined cardiac interventions or in cases of severe, uncontrolled intraoperative bleeding or severe hemodynamic instability. We favor VA ECMO over VV ECMO due to the inability to maintain adequate flow with VV ECMO during hilar exposure due to atrial compression.

During the study period there were no changes in donor organ management. No ex vivo preservation techniques were used in these cases. There were also no differences in patient management or immunosuppression strategy, which comprised standard induction and maintenance therapy based on triple-drug regimen, during the study period.

Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Implantation

The bilateral anteroaxillary thoracotomy has been our preferred surgical approach in double LT. We reserve the clamshell incision to cases with inadequate exposure (severely retracted chest cavity or obesity), increased technical difficulty (multiple thoracotomies or redo LT), or when it is the surgeon's preference.

In the absence of femoral artery calcifications or disease, peripheral cannulation using right femoral vein and artery has been favored in the cases with the minimally invasive approach of using a limited anteroaxillary thoracotomy. Central cannulation in the ascending aorta and right atrium is used in cases with standard clamshell incision or peripheral vascular disease. In patients with preoperative peripheral ECMO as a bridge to LT, maintenance of preoperative cannulation was attempted. Initially, we converted to full CPB; more recently, we have been converting to VA ECMO.

After entering the chest cavity and prior to cannulation, heparinization was used in both groups. In the CPB group, 300 IU heparin/kg was administered to maintain an activated clotting time greater than 400 seconds during bypass. After discontinuation of CPB, protamine was used to reverse the heparin effect. In the ECMO group, an initial bolus of 5,000 IU heparin was given to maintain an activated clotting time 180 to 250 seconds during support. In the ECMO group, protamine administration to revert the heparin effect was only considered after decannulation in cases of significant clinical bleeding manifestations.

The CPB system used included a Stöckert SIII or S5 (Sorin Group GMBH, Munich, Germany) heart and lung machine and roller pump, Terumo Xcoating tubing, Capiox adult hardshell venous reservoir with Xcoating (Terumo CV Corp, Elkton, MD), Capiox RX 2.5 with Xcoating, a hollow fiber oxygenator, and a Capiox adult arterial filter with Xcoating. The ECMO system that we used from July 2007 until March 2012 included CarmedaBioActive surface (Medtronic Inc, Minneapolis, MN) tubing, a BPX-80 centrifugal pump with Carmeda BioActive surface, and a Quadrox i-D oxygenator with Bioline Coating (Maquet Cardiopulmonary AG, Rastatt, Germany). In March 2012, an integrated, hybrid, convertible ECMO and CPB system was implemented using Carmeda tubing, with an Affinity NT adult Carmeda oxygenator (Medtronic Inc), an Affinity NT hardshell cardiotomy reservoir with trillium coating (Medtronic Inc), an Affinity AF1000 arterial filter with balance coating (Medtronic Inc), and a Revolution