Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

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Objective: The study objective was to compare the outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass support in lung transplantation.

Methods: We performed a retrospective cohort study from a prospective database of adult lung transplantations performed at the University of Toronto from 2007 to 2013. Among 673 lung transplantations performed in the study period, 267 (39.7%) required cardiopulmonary support. There were 39 cases of extracorporeal membrane oxygenation (2012-2013) and 228 cases of cardiopulmonary bypass (2007-2013). Patients who were bridged with extracorporeal life support, underwent a concomitant cardiac procedure, received a combined liver or heart transplant, were colonized with *Burkholderia cenocepacia*, or required emergency cannulation for cardiopulmonary support were excluded. Finally, 33 extracorporeal membrane oxygenation cases were matched with 66 cases of cardiopulmonary bypass according to age (±10 years), lung transplantation indication, and procedure type (bilateral vs single lung transplantation).

Results: Recipient factors such as body mass index and gender were not different between extracorporeal membrane oxygenation and cardiopulmonary bypass groups. Furthermore, donor variables were similar, including age, body mass index, last PaO2/FiO2 ratio, smoking history, positive airway cultures, and donor type (brain death and donation after cardiac death). Early outcomes, such as mechanical ventilation requirement, length of intensive care unit stay, and length of hospital stay, significantly favored extracorporeal membrane oxygenation (median 3 vs 7.5 days, $P = .005$; 5 vs 9.5 days, $P = .026$; 19 vs 27 days, $P = .029$, respectively). Perioperative blood product transfusion requirement was lower in the extracorporeal membrane oxygenation group. The 90-day mortality for the extracorporeal membrane oxygenation group was 6% versus 15% for cardiopulmonary bypass ($P = .32$).

Conclusions: Extracorporeal membrane oxygenation may be considered as the first choice of intraoperative cardiorespiratory support for lung transplantation. (J Thorac Cardiovasc Surg 2015;149:1152-7)

See related commentary on pages 1158-60.

Cardiopulmonary bypass (CPB) is the standard and most familiar modality used for intraoperative cardiorespiratory support during lung transplantation (LTx). In most instances CPB is instituted on a selective basis, although there are programs that use it routinely.[1] The theoretic benefit of providing controlled low-pressure reperfusion is obviously counterbalanced by the inflammatory response leading to coagulopathy, neutrophil activation, and complement activation that ultimately lead to end-organ injury.[2] Furthermore, the use of CPB has been highlighted as an independent factor associated with primary graft dysfunction.[3]

In theory, the advantages of extracorporeal membrane oxygenation (ECMO) are a relatively miniaturized circuit that requires lower priming volumes and the lack of both air–blood contact and cardiotomy suction, leading to lesser anticoagulation requirement and potentially to lesser coagulopathy and systemic inflammatory response. In cardiac surgery procedures, the use of a miniaturized CPB circuit has been shown to be associated with lower transfusion requirement, a reduction in peak troponin, and a lower incidence of neurologic damage in comparison with conventional CPB.[4] In a more recent meta-analysis, miniaturized circuits have been shown to have decreased inflammatory response (measured by polymorphonuclear elastase), lesser hemodilution, lesser need for inotropic

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Abbreviations and Acronyms

ACT = activated clotting time
CPB = cardiopulmonary bypass
ECLS = extracorporeal life support
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
LTx = lung transplantation
pRBC = packed red blood cells

support, lower peak creatinine level, lesser need for red blood cell transfusion, and lower incidence of atrial fibrillation. These advantages were reflected in a lower requirement for mechanical ventilation, shorter intensive care unit (ICU) and hospital stay, and ultimately lower hospital mortality.[5]

With all of these findings taken together, one might speculate that ECMO could be a better option for intraoperative support in LTx, an operation that is already marked by a heightened inflammatory milieu. With increasing use of ECMO as a bridge to transplant[6-12] or to recovery in cases of severe primary graft dysfunction,[13-17] some programs have pioneered and expanded its use for the intraoperative period of LTx.[18] Nevertheless, this approach is still underused, and there are only few retrospective reports in the literature addressing this issue.[19]

On the basis of our growing extracorporeal life support (ECLS) experience, in 2012 we started to use venoarterial ECMO instead of CPB for intraoperative support in LTx. In the present study, we compared the outcomes of LTx using ECMO versus CPB using a matched cohort design to reduce the potential for confounding by indication.

MATERIALS AND METHODS

We conducted a retrospective cohort study using a prospective database of patients who underwent LTx from January 2007 to December 2013 and required intraoperative cardiopulmonary support. Cases were labeled as ECMO or CPB and were matched on a 1:2 ratio according to transplant indication, single or double LTx, and age. The latter was frequency matched within a 10-year window. To further reduce the risk of biased inferences, we excluded from the cohort patients who (1) were bridged with ECLS, (2) underwent concomitant cardiac procedure or combined liver or heart transplantation, (3) were colonized with *Burkholderia cenocepacia*, or (4) required emergency cannulation for cardiopulmonary support. Emergency cannulation was defined as institution of CPB because of severe instability during anesthesia induction or massive bleeding. This study was approved by the University Health Network Research Ethics Board.

It has been our practice to use cardiopulmonary support on a selective basis. At the time of the first lung implant, we would institute support in cases of hemodynamic instability or inability to tolerate pulmonary artery clamping or single lung ventilation. In the event that the first lung is implanted without difficulty, then cardiopulmonary support is subsequently initiated if hemodynamic instability or inadequate gas exchange ensues when attempting to support the patient on the newly implanted initial graft. Patients with primary pulmonary hypertension routinely are placed on mechanical support at the initiation of surgery.

The patient population is summarized in Figure 1, *A*. Of 673 LTxs, 39.7% (267) were performed with intraoperative cardiopulmonary support. After the specific exclusion criteria were applied, 33 ECMO cases were matched with 66 CPB cases. The number of cases performed by year, with the correspondent intraoperative support (none, CPB, or ECMO) is shown in Figure 1, *B*. Intraoperative ECMO was first used in 2012 and became the most common mode of intraoperative cardiopulmonary support for LTx within the subsequent year.

Donor and recipient baseline characteristics are shown in Table 1. Donor demographics were similar between groups in terms of age, positive smoking history, and positive bronchoalveolar lavage culture (Table 1). There was a trend to more male donors and more ex vivo lung perfusion use in the ECMO group.

Matching of the recipients was successfully performed according to indication (54% of idiopathic pulmonary fibrosis), type of transplant (85% double lung in CPB vs 82% in ECMO), and age (mean 53.4 $\pm$ 13.5 years for CPB vs 55.8 $\pm$ 12.5 years for ECMO). Gender and body mass index were not different between groups.

Cardiopulmonary Bypass Technique

The traditional CPB system consists of a (1) Stockert S III console (Stockert, Munich, Germany); (2) Medtronic Carmeda BioActive Surface closed venous reservoir (Medtronic Inc, Minneapolis, Minn); (3) Sorin Revolution centrifugal pump (Sorin Group, Mirandola, Italy); (4) Maquet Quadrox-I Adult Softline coated oxygenator (Maquet Cardiopulmonary, Rastatt, Germany) (rated flow 0.5-7.0 L/min, 1.8 m^2 microporous polypropylene gas fiber membrane surface, low prime volume of 215 mL, 0.4 m^2 polyurethane heat exchanger surface area) with a (5) Sorin Physio Micro 27 arterial filter and (6) Sorin Physio tubing pack. Prime volume is minimized to 1.2 L crystalloid (Ringer's lactate). Perfusion technique routinely included a retrograde autologous prime after cannulation when stable hemodynamics permitted, to minimize the circuit crystalloid to 800 mL. Before cannulation, patients were fully heparinized and CPB was instituted with an activated clotting time (ACT) greater than 480 seconds.

Extracorporeal Membrane Oxygenation Technique

The ECLS circuit consisted of (1) a Bio-Medicus centrifugal pump (Medtronic Inc); (2) a Maquet Quadrox-I Adult Softline coated oxygenator (Maquet Cardiopulmonary) (rated flow 0.5-7.0 L/min, 1.8 m^2 microporous polypropylene gas fiber membrane surface, low prime volume of 215 mL, 0.4 m^2 polyurethane heat exchanger surface area); and (3) a Medtronic Carmeda BioActive Surface Tubing (Medtronic Inc). In an effort to optimize patient safety, minimize circuit surface area, and decrease the risk of air entrainment, the circuit was simplified. The bridge was removed, as were pressure isolators and sampling manifolds. The ECLS circuit prime total volume was 800 mL. Before cannulation, patients received 5000 IU of intravenous unfractionated heparin. If an ACT greater than 200 seconds was not achieved, additional heparin was administered to achieve a target ACT of 180 to 200 seconds. ACT is measured every 15 to 30 minutes during the procedure.

Arterial Cannulation

The cannulation sites were selected primarily on the basis of surgeon preference and the type of procedure (single vs double lung transplant). In the cases of central (aortic) cannulation, a 20F to 22F Medtronic cannula was used, according to patient size and predicted cardiac output. In the cases of femoral artery cannulation, 17F to 20F Medtronic cannulae were used using a percutaneous Seldinger, open Seldinger, or cut-down technique. Central cannulation was used in 84% of cases.

Venous Cannulation

Likewise, cannulation sites and type of cannulae were selected on the basis of surgeon preference and transplant type. In cases of central