Use of Extracorporeal Membrane Oxygenation Prior to Lung Transplantation Does Not Jeopardize Short-term Survival

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ABSTRACT

Background. The use of pretransplantation extracorporeal membrane oxygenation (ECMO) has been considered to be a relative contraindication and a risk factor associated with poor outcomes in lung transplantation. However, with a donor shortage, use of ECMO before transplantation is often unavoidable. This study aimed to review our experiences of lung transplantation outcome with regards to the use of pretransplantation ECMO.

Methods. We retrospectively reviewed the clinical data of patients who underwent lung transplantation at our institution. Clinical variables as well as ECMO-related data were analyzed with surgical outcomes.

Results. From 2006 to 2014, 27 patients underwent lung transplantation: 26 bilateral sequential lung transplants and 1 right-side single lung transplant. Of these, 12 (44.4%) received ECMO treatment during the pretransplantation waiting period. Pretransplantation ECMO patients showed higher body mass index scores ($P = .047$) and mechanical ventilation support ($P < .001$) than the non-ECMO group. All ECMO patients were weaned from ECMO after transplantation. The median ECMO runtime was 12 days. The survival-to-discharge rates of the 2 groups did not differ. Survival after lung transplantation at 1, 6, 12, and 24 months was 100%, 73.3%, 61.1%, and 61.1% in the ECMO group and 100%, 86.7%, 86.7%, and 66.0% in the non-ECMO group, respectively ($P = .540$).

Conclusions. Use of pretransplantation ECMO did not jeopardize survival-to-discharge and short-term survival rates in our experience. Our result suggests pretransplantation ECMO can provide a chance of receiving lung transplantation to those who were classified as "too sick to be transplanted."

LUNG TRANSPLANTATION (LTx) is the final rescue method for patients with respiratory failure. According to an International Society for Heart and Lung Transplantation (ISHLT) report, 3719 adult lung transplantations were performed worldwide in 2012, the second highest annual number reported to date since 2011 (3725), the highest activity level [1]. The use of pretransplantation extracorporeal membrane oxygenation (ECMO) or mechanical ventilation (MV) has been considered to be a relative contraindication and a risk factor for poor outcomes after LTx [2]. Based on a retrospective analysis by the United Network for Organ Sharing (UNOS) registry, only

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0.3% patients underwent pretransplantation ECMO and 3.7% underwent MV before transplantation from 1987 to 2008 [2]. Recently, with a shortage of lung donors, the use of ECMO is increasing. Unfortunately, however, many patients who are on ECMO are considered as to be "too sick to be transplanted" and therefore are excluded as transplantation candidates. The purpose of this study is to review our experiences with LTx focusing on the use of pretransplantation ECMO.

MATERIALS AND METHODS

We retrospectively reviewed and analyzed the clinical data of patients who underwent LTx at our institution with regard to underlying lung disease, transplantation-related procedures, hospital death, length of survival, and all data regarding the use of ECMO. Patients who received both heart and lung transplantation were excluded. The study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 1404-147-579).

Selection of Lung Transplant Candidates and ECMO Insertion

The process of selection of LTx candidates was based on international guidelines [3]. Fourteen patients were added to the waiting list at the outpatient clinic. However, 13 patients were listed urgently due to progressive deterioration of respiratory function at the time of being on MV or ECMO support. As those patients usually had several relative contraindications, the decision to list for lung transplantation was made at a multidisciplinary discussion.

Initiation of ECMO support was determined individually by multidisciplinary discussion between pulmonologists, critical care physicians, and thoracic surgeons, based on Extracorporeal Life Support Organization guidelines [4]. The relative contraindications of ECMO support are short expected survival owing to pre-existing conditions such as malignancy, conditions incompatible with normal life even if the patient recovered such as irreversible neurologic damage, and uncontrollable systemic bleeding. Venovenous (VV) ECMO was commonly used for respiratory support. Percutaneous insertion using Seldinger's technique was performed on most adult patients. Femoral veins and/or internal jugular veins were used for VV ECMO. Heparin was the most commonly used anticoagulant agent, and activated clotting time or activated partial thromboplastin time was used to monitor the anticoagulation level. Respiratory function was determined based on the Pao_2/Fio_2 ratio and $Paco_2$. We analyzed the last arterial blood gas analysis result before application of invasive respiratory support (for the MV group, the last result just before intubation; for the ECMO group, the last result just before ECMO application; and for the nonsupport group, the worst result before LTx). All ECMO procedures were performed by thoracic surgeons.

Surgical Procedures and Donor Preservation in Lung Transplantation

Donor organ assessment was performed with radiological examination, arterial blood gas analysis, bronchoscopy, assessment of chest compliance, and visual inspection of the lungs. After confirmation of donor lung suitability, the recipient was prepared for LTx. The recipient underwent a clamshell incision through the fourth intercostal space. During the surgical procedure, cardiopulmonary bypass was used for hemodynamic support in most patients. ECMO was maintained during the surgical procedure with low flow rates, and the weaning of ECMO was determined intraoperatively after the lung anastomosis was accomplished. Cold ischemic time was defined as the time interval between the application of the aortic crossclamp during harvesting and the reperfusion after anastomosis.

Data Analysis

Continuous variables are presented as median values with an interquartile range (IQR), and categorical variables are expressed as frequency and proportion if not otherwise specified. Comparisons between groups were analyzed using the Pearson χ^2 test or Fisher's exact test for categorical variables, and the Mann-Whitney U test or Kruskal-Wallis test for continuous variables. A P value $< .05$ was considered statistically significant. Kaplan-Meier analysis was used to calculate cumulative survival, and the log-rank test was used to compare survival between the groups.

RESULTS

Patient Demographics

From 2006 to 2014, 27 patients underwent lung transplantations: 26 bilateral sequential lung transplantations and 1 right single LTx. Fifteen patients were male. Interstitial lung disease, with or without underlying connective tissue disease, was the most common underlying disease (59.3%), followed by bronchiectasis (14.8%) and lung diseases after bone marrow transplantation (14.8%). The baseline characteristics of each group are described in Table 1. Of the 27 patients, 17 patients were under MV support and 11 patients required tracheostomy during the waiting period prior to transplantation. Eleven patients (40.7%) were urgently listed for LTx after initiation of MV. Pretransplantation ECMO was used on 12 patients. In the pretransplantation ECMO group, 7 patients (58.7%) were added to the waiting list for LTx after intubation, and the remaining 5 patients were listed on 1, 5, 19, 22, and 90 days before MV application. The median waiting time from registration to LTx was significantly shorter in the ECMO group than that in the non-ECMO group (16 days (IQR, 8–48 days) vs 38 days (IQR, 26–90 days, $P = .025$). the ECMO group showed poorer respiratory function despite of advanced MV support with a median Pao_2/Fio_2 (fraction of inspired oxygen) ratio of 60.5 mm Hg (IQR, 46.4–65.4 mm Hg) than the non-ECMO group ($P < .001$).

Pretransplantation ECMO Usage

Twelve patients required ECMO support as a bridge to LTx. Patients undergoing ECMO had a significantly higher body mass index (BMI) ($P = .047$, median 21.2 kg/m^2 in the ECMO group vs 17.9 kg/m^2 in the non-ECMO group) and a more frequent requirement for MV support ($P < .001$) than non-ECMO patients (Table 1). The duration of preoperative MV support was not significantly different between the ECMO group and the non-ECMO group ($P = .196$, median 18 days in the ECMO group [n = 12] vs 27 days in the non-ECMO group [n = 7]). Three patients were weaned off ECMO intraoperatively and the remaining 9 patients were successfully weaned off after LTx. Two patients in the non-ECMO group required postoperative ECMO support due to primary graft failure. The median duration of ECMO