Continued Utility of Single-Lung Transplantation in Select Populations: Chronic Obstructive Pulmonary Disease

Daine T. Bennett, MD, Martin Zamora, MD, T. Brett Reece, MD, John D. Mitchell, MD, Joseph C. Cleveland, Jr, MD, Frederick L. Grover, MD, Ashok N. Babu, MD, Robert A. Meguid, MD, MPH, David A. Fullerton, MD, and Michael J. Weyant, MD

Department of Surgery, Division of Cardiothoracic Surgery and Department of Medicine, Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado Denver, Anschutz Medical Campus, Aurora, Colorado

Background. **The use of single lung transplantation (SLTx) for chronic obstructive pulmonary disease is often viewed as inferior therapy compared with bilateral lung transplantation (BLTx). We hypothesized from our experience that subpopulations of recipients with emphysema exist in which SLTx represents therapy that is equivalent to BLTx, therefore allowing more patients access to transplantation.**

Methods. **Consecutive patients undergoing LTx for emphysema between 1992 and 2012 at a single institution were identified and analyzed retrospectively. A similar cohort from the United Network of Organ Sharing (UNOS) national database was identified for comparison. Five-year survival in patients receiving SLTx and those receiving BLTx were compared using Kaplan-Meier survival curves and log-rank tests.**

Results. **Two hundred thirty-six patients meeting criteria were identified from our institution. Two hundred six underwent SLTx, and 30 underwent BLTx. Five-year survival for single-center SLTx (53.2% ± 3.6%) and BLTx (56.7% ± 10.2%) was not significantly different ($p = 0.753$). The national database included 7,256 patients meeting selection criteria, with 4,408 undergoing SLTx and 2,848 undergoing BLTx. Five-year survival among the national cohorts was lower for SLTx (46.4% ± 0.8%) compared with BLTx (55.9% ± 1.1%) ($p < 0.0001$). However, 5-year survival for our single-center SLTx experience (53.2% ± 3.6%) was comparable to the national BLTx cohort (55.9% ± 1.1%) ($p = 0.539$).**

Conclusions. **Five-year survival after SLTx for emphysema was comparable to that for BLTx in cohorts from our institution and from the UNOS national database. Further study should focus on the mechanism behind these improved outcomes. Given the potential for a larger number of life-years saved, SLTx should continue to be considered a therapeutic option in appropriately selected patients with chronic obstructive pulmonary disease (COPD).**

(Ann Thorac Surg 2015;■:■–■)

The wait-list mortality for lung transplantation (LTx) is currently on the rise, with a mortality rate of 15.4 individuals per 100 wait-list years [1]. Efforts to broaden the donor pool through the use of extended donors, such as cardiac death donors, and ex vivo lung perfusion techniques have shown acceptable success [2]. Despite these efforts, we continue to face a donor shortage. There remains a need for improved use of available donor lungs to combat the worsening wait-list mortality. When appropriate, the use of single lung transplantation (SLTx) instead of bilateral lung transplantation (BLTx) has the potential to increase the pool of donor lungs and improve the survival for a larger population of patients awaiting LTx. In addition, donors frequently are only able to produce a single lung for transplantation because of injurious mechanisms in the contralateral lung. Transplantation of appropriate recipients with single lungs such as these could also improve wait-list times for those patients who require BLTx.

LTx for chronic obstructive pulmonary disease (COPD) was initially perceived to require BLTx because of the potential for a severe ventilation/perfusion mismatch and hyperinflation of the native lung compressing the donor lung [3]. In the early 1990s, reports emerged demonstrating that SLTx was feasible in patients with COPD [4, 5]. Subsequent small series of patients found comparable survival outcomes between SLTx and BLTx [6, 7]. More recently, large single-center reviews and national database studies have shown an individual survival benefit for BLTx compared with SLTx in patients with COPD, leading some practitioners to advocate for the use of BLTx only [8, 9]. However, in select populations with COPD, survival outcomes are comparable for SLTx and BLTx [10, 11].

Our institution advocates the continued use of SLTx for patients with COPD, specifically older individuals, which

Accepted for publication March 10, 2015.

Presented at the Sixty-first Annual Meeting of the Southern Thoracic Surgical Association, Tucson, AZ, Nov 5–8, 2014.

Address correspondence to Dr Weyant, Section of General Thoracic Surgery, Division of Cardiothoracic Surgery, University of Colorado Denver School of Medicine, 12631 East 17th Ave, MS C310, Aurora, CO 80045; e-mail: michael.weyant@ucdenver.edu.

Published by Elsevier

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2015.03.024

has been the practice since the inception of our institution's LTx program. We typically offer SLTx to patients older than 55 years, whereas BLTx remains favored for younger recipients in all disease groups. The purpose of this study was to compare survival of SLTx recipients to BLTx recipients with end-stage COPD through a retrospective analysis of patients treated at our institution. We hypothesized that 5-year survival would not be significantly different among the 2 cohorts. We also compared survival at the single center to comparable groups from a national database. The results of this study demonstrate comparable 5-year survival among the single-center SLTx cohort and BLTx recipients at both the local and national levels.

Patients and Methods

Patient Population

The records of all patients undergoing SLTx or BLTx for COPD at our institution from January 1, 1992 to December 31, 2012 were retrospectively reviewed. Patients undergoing repeated transplantation or transplantation for alpha-1 antitrypsin deficiency were excluded. We favor BLTx for patients with alpha-1 antitrypsin deficiency because we have seen increased rates of acute native lung hyperinflation with SLTx in this subgroup [12]. Patients with the same criteria were identified in the United Network for Organ Sharing (UNOS) Transplant Analysis and Research file for the years 1992-2012 for comparison. The Colorado Multiple Institutional Review Board approved the protocol for review of patient information with protocol No. 13-0080.

Survival Analysis

Single-center and UNOS data were analyzed with IBM SPSS Statistics, version 22.0 (SPSS Inc, Chicago, IL). Preoperative patient characteristics were compared using an unpaired t test for continuous variables and Pearson's χ^2 test for categorical variables to evaluate preoperative differences between groups. For both the single-center and UNOS data, survival was calculated from time of transplantation until death. Survival estimates between SLTx and BLTx were calculated using Kaplan-Meier curves and statistically compared using the Mantel-Cox log-rank test. Thirty-day, 1-year, and 5-year survival rates are reported. Five-year survival between single-center SLTx and UNOS BLTx are further analyzed with a multivariate Cox proportional hazard regression model to adjust for potential confounding factors of survival. Variables included in this analysis are single-center SLTx versus UNOS BLTx, age, forced expiratory volume in 1 second (FEV_1), oxygen requirement at rest, and sex.

Years of Survival per Donor

This study also sought to evaluate the total survival benefit gained from a single donor who supplied lung allografts to 2 separate recipients. To accomplish this, we identified all paired recipients who received single lung transplants from an individual donor as well as those who received bilateral lung transplants. For each pair of single lung transplants, at least 1 of the 2 recipients carried the diagnosis of COPD, and all BLTx recipients were diagnosed with COPD. All repeated transplantations were excluded. Median total years of survival for paired SLTx recipients from a single donor were compared with BLTx recipients using a Mann-Whitney U test with associated interquartile ranges. To allow at least a 5-year follow-up time, patients receiving lung transplants after December 31, 2007 were excluded.

Results

Five-Year Survival: SLTx Versus BLTx at a Single Institution

Between 1992 and 2012, a total of 564 LTx procedures were performed at our institution. There were 236 patients who underwent LTx for COPD, after excluding all patients with a diagnosis of alpha-1 antitrypsin deficiency and all repeated transplantations. A total of 206 recipients received SLTx, and 30 patients received BLTx. Preoperative characteristics of this single-center cohort were comparable between SLTx and BLTx recipients (Table 1), with no significant difference in FEV_1, forced vital capacity, mean pulmonary artery pressure, 6-minute walk distance, albumin level, or body mass index. Patients who received SLTx were significantly older, by more than 6 years, at the time of transplantation ($p < 0.0001$), which follows our practice pattern of performing BLTx in younger patients.

Kaplan-Meier survival curves demonstrated similar estimates of survival between SLTx and BLTx recipients in the single-center data. The 30-day, 1-year, and 5-year survival estimates with standard deviation were 96.7% $\pm$ 1.1%, 88.3% $\pm$ 2.2%, and 53.2% $\pm$ 3.6% for SLTx recipients and 96.7% $\pm$ 3.3%, 90.0% $\pm$ 5.5%, and 56.7% $\pm$ 10.2% for BLTx recipients (Fig 1). Although the BLTx recipients demonstrated slightly higher survival at 5 years, this difference was not significant ($p = 0.753$).

Five-Year Survival: Single-Center SLTx Versus UNOS BLTx

Given the limited number of patients who received BLTx for COPD at our institution, we compared SLTx from our single-center data to lung transplant recipient survival from the national UNOS database. There were 2,848 BLTx recipients and 4,408 SLTx recipients available for review in the UNOS database (years 1992–2012) who met the same inclusion criteria applied to the single-center group. Many of the preoperative demographics were significantly different among single-center SLTx and UNOS BLTx (Table 1). On average, SLTx recipients from the single-center data were older and exhibited lower values for pulmonary function tests, 6-minute walk distances, and serum albumin levels. Given these data, the cohort of patients from the single-center cohort demonstrated a preoperative risk that was at least similar to if not higher than the UNOS cohort.

Thirty-day, 1-year, and 5-year survival estimates with standard deviation by Kaplan-Meier curves in the UNOS database cohorts were 95.1% $\pm$ 0.3%, 81.1% $\pm$ 0.6%, and