

# Impact of bilateral versus single lung transplantation on survival in recipients 60 years of age and older: Analysis of United Network for Organ Sharing database

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**Objective:** Lung transplantation has been increasingly applied to patients over the age of 60 years. Importantly, the procedure of choice, single versus bilateral lung transplantation, remains unclear. Therefore, the purpose of this study was to examine short- and midterm outcomes in this age group with particular attention to procedure type.

**Methods:** All first lung transplant recipients, 60 years of age or older, reported to the United Network for Organ Sharing from 1998 to 2004 were divided into two groups: bilateral and single lung transplantation. A retrospective review of pertinent baseline characteristics, clinical parameters, and outcomes was performed. Kaplan–Meier methodology was used to estimate and Cox proportional hazards regression modeling was used to compare posttransplant survival between these groups. Additionally, propensity scores analysis was performed.

**Results:** During the study period, 1656 lung transplant recipients were 60 years of age or older (mean  $62.7 \pm 2.4$  years, median 62 years). Of these, 364 (28%) had bilateral and 1292 (78%) had single lung transplantation. Survival was not statistically different between the two groups. In the multivariate analysis, bilateral versus single lung transplantation was not a predictor of mortality. Idiopathic pulmonary fibrosis and a donor tobacco history of more than 20 pack-years were significantly associated with mortality ( $P = .003$ , CI 1.12–1.76; and  $P = .006$ , CI 1.09–1.63; respectively).

**Conclusions:** The survival of lung transplant recipients 60 years of age or older who underwent bilateral versus single lung transplantation is comparable. These data suggest that type of procedure is not a predictor of mortality in this age group. Idiopathic pulmonary fibrosis and donor cigarette use of more than 20 pack-years were independently associated with mortality.

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**R**esults of clinical lung transplantation (LTx) over the past two decades have progressively improved. Nonetheless, LTx is limited by the availability of donor organs, and a careful selection of LTx recipients is critically important. The International Society for Heart and Lung Transplantation (ISHLT) guidelines for selection of appropriate candidates for LTx have suggested an age limit of 60 years for bilateral (BLT) and 65 years for single (SLT) lung transplantation.<sup>1</sup> The age limitation was based on previous reports showing that older patients have significantly higher mortality than younger patients.<sup>2</sup> However, the age distinction for BLT versus SLT has not been clearly supported by the literature. The few reports that address this issue have been limited to disease-specific database analyses<sup>3,4</sup> and a single-center report with a small number of patients.<sup>5</sup>

As the number of older patients listed for LTx increases, the procedure of choice (BLT vs SLT) for these patients requires further scrutiny. We therefore analyzed the impact of procedure type on short- and midterm survival in recipients 60 years of age

**Abbreviations and Acronyms**

- BLT = bilateral lung transplantation
- COPD = chronic obstructive pulmonary disease
- FVC = forced vital capacity
- IPF = idiopathic pulmonary fibrosis
- ISHLT = International Society for Heart and Lung Transplantation
- LTx = lung transplantation
- SLT = single lung transplantation
- STAR = Standard Transplant Analysis and Research (files)
- UNOS = United Network for Organ Sharing

or older for all disease types, using data reported to the United Network for Organ Sharing (UNOS) registry in the recent era, between 1998 and 2004.

**Materials and Methods**

**Patient Population**

Data reported to the UNOS registry for LTx performed between January 1, 1998 and December 31, 2004 were analyzed. The follow-up period was up to September 2005, which is when the files were created. This time period was chosen to represent a modern cohort of patients in light of advancements made in LTx. Among the 6785 first-time LTx recipients, we identified 1656 patients 60 years of age or older, and these were stratified by type of transplant procedure: BLT (n = 364) and SLT (n = 1292). The patient characteristics are shown in Table 1.

**Statistical Analyses and Survival**

All available data from the UNOS Standard Transplant Analysis and Research (STAR) files were imported into Stata version 9.0 (Stata-Corp. College Station, Tex), which was used for statistical computations. Continuous variables are summarized as mean ± standard deviation. Bivariate comparison of continuous variables was per-

formed with a Student *t* test. Associations between categorical variables were tested by the Pearson  $\chi^2$  test. Survival estimates for each procedure type were calculated by the Kaplan–Meier method, and statistical differences between survival curves were assessed by the log–rank (Mantel–Cox) test. Multivariate analyses were performed by Cox proportional hazards regression to determine whether type of procedure was an independent predictor of mortality after adjustment for potential cofounders. During the analyses for model selection, only variables with more than two thirds of available data were considered, and these are listed in Table 2. To more accurately estimate confidence intervals, we made the assumption that the missing data were missing at random and performed imputation of missing data using the single regression method. Our findings proved to be robust across models that included both imputed and nonimputed (ie, case-wise deletion of observations with missing data points) data. We therefore chose to construct a model that reflects the effect of the clinically relevant potential cofounders listed in Table 2. This model also has the lowest Akaike and Schwarz Bayesian information criterion scores, which makes it a model of choice.

In addition to the standard multivariate analysis, to reduce bias and increase precision, we generated propensity scores by developing a model that estimates the probability of a patient receiving BLT versus SLT. The factors used in this model were recipient age, donor age, body mass index, pulmonary artery mean pressure, forced vital capacity (FVC) (percent predicted), and year of transplant. Propensity scores were analyzed by the regression adjustment technique; that is, both the propensity scores and type of procedure (“treatment factor”) were included in a Cox regression model.

**Results**

**Patient Characteristics**

Of the 1656 first LTx recipients, 364 patients received BLT and 1292 had SLT. Their ages ranged from 60 to 87 years old (mean 62.7 ± 2.4 years, median 62 years). The age distribution is shown in Figure 1. Eighty-eight percent of the patients were between 60 and 65 years old. Interestingly, there were 196 patients (12%) above the age of 65 years. Furthermore, from

**TABLE 1. Clinical characteristics by type of procedure**

Clinical characteristics	BLT (N = 364)	No. with data	SLT (N = 1292)	No. with data	P value
Age (y)	62.3 ± 2.1	364	62.8 ± 2.5	1292	.002
Female gender	134 (37%)	364	553 (43%)	1292	.004
Donor age (y)	32.1 ± 14.4	364	32.8 ± 13.8	1291	.4
Native disease		364		1292	<.001
COPD	224 (62%)		863 (67%)		
IPF	80 (22%)		349 (27%)		
Others	60 (16%)		80 (6%)		
BMI	24.1 ± 3.9	356	25.2 ± 6.2	1220	<.001
FEV <sub>1</sub> (%)	35.5 ± 23.4		34.5 ± 20.6		.66
FVC (%)	55.5 ± 17.9	340	53.1 ± 16.3	1162	.025
Mean PAP (mm Hg)	26.2 ± 8.1	281	24.7 ± 8.5	1002	.01
Ischemia time (h)	5.3 ± 1.6	322	3.78 ± 1.3	1107	<.001
Follow-up time (mo)	21 ± 19	364	26 ± 21	1291	.001

BLT, Bilateral lung transplantation; SLT, single lung transplantation; COPD, chronic obstructive pulmonary disease; IPF, idiopathic pulmonary fibrosis; BMI, body mass index; FEV<sub>1</sub> (%), forced expiratory volume (percent predicted); FVC, forced vital capacity; PAP, pulmonary artery pressure.

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