Lung transplantation in patients 70 years old or older: Have outcomes changed after implementation of the lung allocation score?

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Objective: The objective of the present study was to evaluate whether the outcomes of lung transplantation in patients aged 70 years or older have changed after implementation of the lung allocation score in May 2005.

Methods: Patients aged 70 years or older undergoing primary lung transplantation from 1995 to 2009 were identified from the United Network for Organ Sharing registry. The primary stratification was the pre-lung allocation score era versus lung allocation score era. Risk-adjusted multivariate Cox regression and Kaplan-Meier analyses were conducted to evaluate the effect of age 70 years or older on 1-year post-transplant mortality compared with a reference cohort of patients aged 60 to 69 years.

Results: Of the overall 15,726 adult lung transplantation patients in the study period, 225 (1.4%) were 70 years old or older and 4634 (29.5%) were 60 to 69 years old. The patients aged 70 years or older were a larger cohort of overall lung transplantation patients in the lung allocation score era compared with before the lung allocation score era (3.1% vs 0.3%, $P < .001$). In the risk-adjusted Cox analysis, age 70 years or older was a significant risk factor for 1-year post-lung transplantation mortality in the pre-lung allocation score era (hazard ratio, 2.00; 95% confidence interval, 1.10-3.62, $P = .02$) but not in the lung allocation score era (hazard ratio, 1.02; 95% confidence interval, 0.71-1.46; $P = .92$). Similarly, Kaplan-Meier 1-year survival was significantly reduced in patients 70 years old or older versus 60 to 69 years old in the pre-lung allocation score era (56.7% vs 76.3%, $P = .006$) but not in the lung allocation score era (79.0% vs 80.0%, $P = .72$).

Conclusions: Recipients aged 70 years or older were a larger proportion of overall lung transplantation patients after implementation of the lung allocation score. Although associated with significantly increased post-lung transplantation mortality in the pre-lung allocation score era, age 70 years or older is currently associated with outcomes comparable to those of patients aged 60 to 69 years. Therefore, age 70 years or older should not serve as an absolute contraindication to lung transplantation in the lung allocation score era. (J Thorac Cardiovasc Surg 2012;144:1133-8)

GTS

With an aging population in the United States, the number of patients with end-stage lung disease will undoubtedly continue to increase. This again brings into question the long debated issue of what the upper age limit should be for recipients of lung transplantation (LTx). A consensus report published in 2006 from the International Society for Heart and Lung Transplantation recommended that recipient age older than 65 years should serve as a relative contraindication to LTx.[1] This recommendation was based on International Society for Heart and Lung Transplantation registry data demonstrating reduced survival in this elderly cohort.[2] It is unknown whether the implementation of the lung allocation score (LAS) in May 2005 has been met with any changes in outcomes after LTx in elderly recipients. In the present study, we evaluated the trends and outcomes of LTx in recipients aged 70 years or older in the United States.

PATIENTS AND METHODS

Data Source

The United Network for Organ Sharing (UNOS) data set was used for the present study. The UNOS registry collects patient-level data on all transplantations performed in the United States. The Johns Hopkins University School of Medicine approved our study.

Study Population

All adult patients (age > 17 years) undergoing LTx between January 1, 1995, and December 31, 2009 were initially identified in the UNOS data set. Patients undergoing multivisceral transplantation, including heart–lung transplantation, were excluded. Redo lung transplants were also excluded from the analysis.

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Abbreviations and Acronyms
LAS = lung allocation score
LTx = lung transplantation
UNOS = United Network for Organ Sharing

Trends in LTx in Elderly Recipients

To examine nationwide trends, we stratified the recipients into 3 age groups: 18 to 59 years, 60 to 69 years, and 70 years old or older. The absolute number of recipients within each of these age cohorts was then plotted for each year during the study period. The trends were then evaluated by calculating the correlation coefficients (r) and the associated P values.

We also compared the trends in key baseline characteristics of elderly recipients. Moreover, the recipient, donor, and transplant variables for recipients aged 70 years or older were compared between those who underwent transplantation in the pre-LAS era versus the LAS era. These included the following recipient variables: age, gender, race, weight, height, body mass index, etiology of lung disease, recent infection, dialysis while on the wait list, serum creatinine, serum bilirubin, serum cytomegalovirus positivity, bridging with extracorporeal membrane oxygenation, mechanical ventilation before transplantation, intensive care unit before transplantation, diabetes mellitus, hypertension, previous malignancy, and blood transfusion while on the wait list. Donor variables that were compared included age, gender, race, weight, height, body mass index, serum cytomegalovirus positivity, cigarette use, diabetes mellitus, terminal creatinine, hypertension, inotrope use, and mechanism of death. The transplant variables included transplant type (single versus bilateral LTx), days on the wait list, ischemic time, and center volume. Pairing data between the recipient and donor included gender matching, race matching, blood type matching, donor/recipient body mass index ratio, donor/recipient weight ratio, donor/recipient height ratio, human leukocyte antigen matching, and cytomegalovirus status matching.

Risk-Adjusted Cox Regression Analysis

Multivariate Cox regression models were constructed to examine the risk-adjusted effect of recipient age 70 years or older on 1-year all-cause mortality after LTx. The reference cohorts in these analyses were recipients aged 60 to 69 years. Risk adjustment was performed for the recipient, donor, and transplant variables that were associated with 1-year mortality on exploratory univariate analysis ($P < .2$) and had less than 20% missing data. All the variables listed previously were tested in this exploratory analysis for potential inclusion in the multivariate models. Significant interactions between covariates were thoroughly tested.

Kaplan-Meier Survival Analysis

Kaplan-Meier survival curves were also constructed. These curves were stratified according to age cohort (age 60-69 years vs age $\geq$70 years) and era (pre-LAS era vs LAS era). The log-rank test was used to compare the survival curves between the age groups within each era.

Statistical Analysis

The categorical data are presented as the number and percentage and were compared using the chi-square test or Fisher's exact test. Continuous data are presented as the mean $\pm$ standard deviation and were compared using the Student t test. All statistical analyses were performed using STATA, software version 11 (StataCorp, College Station, Tex).

RESULTS

Study Cohort

A total of 16,823 adult patients underwent LTx from 1995 to 2009 in the UNOS data set. Of these, 562 were re-do LTx, 495 were heart–lung transplants, and 40 were other types of multivisceral transplants. After excluding these cases, 15,726 adult first-time, single-organ LTx patients were included in the study. Of these, 225 (1.4%) were 70 years old or older and 4634 (29.5%) were 60-69 years old.

Trends in LTx in Elderly Recipients

Several significant trends were observed with regard to recipient age during the study period. The proportion of adult LTx recipients aged 18 to 59 years decreased significantly from 85.0% in 1995 to 52.5% in 2009 ($P < .001$; Figure 1). During the same period, the proportion of recipients aged 60 to 69 years increased from 14.8% to 43.0% and the proportion of recipients aged 70 years or older increased from 0.3% to 4.5% ($P < .001$). When stratified according to the implementation of the LAS, the proportion of LTx recipients who were 70 years or older increased from 0.3% (n = 30 of 9,338) in the pre-LAS era to 3.1% (n = 195 of 6391) in the LAS era ($P < .001$).

Baseline Characteristics

Also, significant trends were seen when comparing the baseline characteristics of recipients aged 70 years or older in the pre-LAS versus the LAS era. Moreover, septuagenarian recipients in the LAS era were older (Table 1). The mean serum creatinine level in the LAS group was significantly lower than in the pre-LAS cohort, although no patients in either septuagenarian cohort underwent dialysis while on the wait list. Similar to previous data examining the effect of the LAS for all LTx patients, elderly LTx patients in our study in the LAS era had shorter wait list times and a greater proportion were patients with idiopathic pulmonary fibrosis with fewer having chronic obstructive pulmonary disease. The mean LAS in the septuagenarian LTx recipients in the modern cohort was 47.2 $\pm$ 16.0.

The donors for septuagenarian recipients were well-matched between eras (Table 2). The recipient–donor pairing data were also comparable. Centers performing LTx in recipients aged 70 years or older had significantly greater volumes in the LAS era than in the pre-LAS era, performing on average 9 more LTx annually.

Risk-Adjusted Cox Regression Analysis

On univariate Cox regression analysis, recipients aged 70 years or older were more than twice as likely to die within 1 year of LTx as recipients aged 60 to 69 years in the pre-LAS era (hazard ratio, 2.13; 95% confidence interval, 1.23-3.70; $P = .007$). In the LAS era, age 70 years or older was not a significant risk factor for 1-year mortality on univariate analysis (hazard ratio, 1.06; 95% confidence interval, 0.77-1.47; $P = .72$). Similar trends were observed after risk adjustment for significant recipient, donor, and transplant variables in the pre-LAS versus LAS eras.