Survival in Adult Lung Transplant Recipients Receiving Pediatric Versus Adult Donor Allografts

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Background. **Recent evidence showed that pediatric donor lungs increased rates of allograft failure in adult lung transplant recipients; however, the influence on survival is unclear.**

Methods. **The United Network for Organ Sharing (UNOS) database was queried from 2005 to 2013 for adult lung transplant recipients (≥18 years) to assess survival differences among donor age categories (<18 years, 18 to 29 years, 30 to 59 years, ≥60 years).**

Results. **Of 12,297 adult lung transplants, 12,209 were used for univariate Cox models and Kaplan-Meier (KM) analysis and 11,602 for multivariate Cox models. A total of 1,187 adult recipients received pediatric donor lungs compared with 11,110 receiving adult donor organs. Univariate and multivariate Cox models found no difference in survival between donor ages 0 to 17 and donor ages 18 to 29, whereas donor ages 60 and older were significantly associated with increased mortality hazard, relative to the modal category of donor ages 30 to 59 (adjusted hazard ratio = 1.381; 95% confidence interval = 1.188% to 1.606%; $p < 0.001$). Interactions between recipient and donor age range found that the oldest donor age range was negatively associated with survival among middle-aged (30 to 59) and older (≥60) lung transplant recipients.**

Conclusions. **Pediatric donor lung allografts were not negatively associated with survival in adult lung transplant recipients; however, the oldest donor age range was associated with increased mortality hazard for adult lung transplant recipients.**

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Lung transplantation (LTx) is the only treatment option for end-stage lung disease. Because the organ demand exceeds the supply, there is a substantial mortality rate among patients awaiting LTx [1, 2]. Owing to these limitations, various strategies are used to optimize or increase organ availability, such as extended-criteria donors, donation after cardiac death, ex-vivo perfusion systems to recondition marginal organs, and international resource-sharing arrangements [2–11].

In the United States, donors for LTx are considered from a wide age range, with no restrictions according to the current allocation process [12]. The majority of published work regarding the effects of donor age has centered on older donor lungs, which have been shown to adversely influence outcomes after LTx [13, 14]. Baldwin and colleagues [13] reported that recipients of lungs from donors 65 years old and older had increased rates of 1-year graft failure, and recent work [14] by our group found that lungs from older donors (≥50 years of age) were adversely related to survival in younger recipients younger than 60 or younger than 65 years. In pediatric LTx recipients, adult donor lung allografts were not associated with worse survival [15].

In their work, Baldwin and colleagues [13] reported that recipients of lungs from donors younger than 18 years had increased rates of 1-year graft failure (adjusted hazard ratio [HR] = 1.23; 95% confidence interval [CI] = 1.01% to 1.50%). To date, no study has investigated whether pediatric donor lungs affect survival in adult recipients. Therefore, we sought to examine whether allografts from pediatric lung donors influenced survival in adults undergoing LTx, using an available database in the United States while also comparing recipient survival across three age ranges of adult donors.

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Material and Methods

Data Collection

We retrospectively evaluated data from LTx recipients who were registered in the Organ Procurement and Transplant Network (OPTN) Standard Transplant Analysis and Research Database administered by the United Network for Organ Sharing (UNOS) [5]. The study was approved by The Ohio State University Wexner Medical Center Institutional Review Board with a waiver of the need for individual consent (IRB#2012H0306). The UNOS/OPTN thoracic database was queried for all LTX procedures performed since the implementation of the lung allocation score from May 2005 to September 2013.

Statistical Methods

All analyses were performed with Stata/MP, version 13.1 (College Station, TX: StataCorp LP). For all analyses, a p value <0.05 was considered statistically significant.

Descriptive statistics for continuous variables were presented as medians and interquartile ranges, and descriptive statistics for categoric variables were presented as counts and percentages. To assess the effects of lung donor age in adult LTx recipients, we categorized donor age as below 18 (ie, 0 to 17) years, 18 to 29 years, 30 to 59 years, or 60 years and older. In a univariate Cox proportional hazards model of survival after LTx, there were no significant differences in survival between donor age ranges 0 to 13 and 14 to 17 years, or among donor age ranges 30 to -39, 40 to 49, and 50 to 59 years. Therefore, these donor age ranges were collapsed into 0 to 17 and 30 to 59 years, respectively.

Survival duration was analyzed from the date of the transplantation until the date of death or censoring. The time metric was days of survival until death or censoring. Kaplan-Meier survival curves were calculated to show LTx patient survival in each of the four categories of donor age, with a log-rank test identifying any statistically significant difference among these four survival functions. Univariate Cox proportional hazards regression models were used to assess the relationship between donor age and each covariate and the hazard of mortality after LTx.

Multivariate Cox proportional hazards models were then fitted, with adjustment for a series of characteristics, including donor and recipient gender and race, and other recipient characteristics (diagnosis, age, creatinine, and body mass index [BMI]), donor height, and allograft ischemic time. In a first model, all covariates were entered into the multivariate model. In a second model, forward and backward selection was used to construct the multivariate model, with inclusion or exclusion criteria of $p < 0.200$, respectively. (Forward and backward selection resulted in the same model, as shown below). In a final model, donor age categories were interacted with recipient age categories to examine which combinations of donor and recipient age were most predictive of mortality after LTx and to test whether the relationship between donor age category and survival persisted within each recipient age category.

Results

Study Population

Supplemental Figure 1 presents the inclusion and exclusion criteria for our study. Of all 136,498 organ transplant candidates, 12,297 first-time adult recipients who underwent LTx no earlier than May 2005 were identified. Exclusion criteria included patients with age younger than 18 years, no LTx date, LTx performed before May 2005, history of prior LTx, and noncadaveric donor. Further exclusion criteria included identical dates of transplantation and death or censoring for survival analysis, and missing covariate data for multivariate survival analysis.

Table 1 summarizes the characteristics of the adult LTx recipients with a comparison between donor ages 0 to 17 years and donor ages 18 or older. Of the 12,297 recipients included in the study, 1,187 received pediatric (ages 0 to 17) donor lungs, including 183 recipients of lungs from donor ages 0 to 13 years. Meanwhile, 11,110 received adult organs, with a majority of this group (55%) receiving organs from donor ages 30 to 59 years. Male recipients were more likely to receive allografts from an adult donor, whereas male donors were more common in the group of patients receiving allografts from donors younger than 18 years old. In the entire sample and each donor age category, both recipients and donors were predominantly white. Diagnosis categories that were overrepresented in the pediatric donor lung group included primary pulmonary hypertension, cystic fibrosis, sarcoidosis, and α-1 antitrypsin deficiency. Adult LTx recipients receiving pediatric donor lungs were more likely to be between 18 and 29 years of age and to have a lower BMI. There were no significant differences in creatinine and allograft ischemic time between the two groups.

Univariate and Kaplan-Meier Survival Analysis

A total of 12,209 patients were included in the univariate Cox and Kaplan-Meier survival analysis. Analysis of donor age categories found no difference in survival between donor ages 0 to 17 and 18 to 29, but a significant increase in mortality hazard among recipients with donors age 60 or older, relative to donor ages 30 to 59 (HR = 1.382; 95% CI = 1.193% to 1.601%; p <0.001) (Table 2, Fig 1). Greater donor height was associated with a lower hazard of mortality (HR = 0.995; 95% CI = 0.992% to 0.998%; $p = 0.002$).

Multivariate Survival Analysis

A total of 11,602 patients were included in the multivariate survival analysis. Table 3 outlines the Cox proportional hazards models, with model 1 including all covariates and model 2 including only those covariates meeting the forward or backward selection criteria (forward and backward selection of covariates resulted in the same model specification). As with the univariate analysis, model 1 shows that the oldest donor age range, 60 and older, was associated with a significantly higher mortality hazard than was the 30 to 59 donor age range