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Influence of donor and recipient age in lung transplantation

Don Hayes Jr., MD, MS,[a,b,c] Sylvester M. Black, MD, PhD,[d] Joseph D. Tobias, MD,[e,f] Robert S. Higgins, MD, MSHA,[d] and Bryan A. Whitson, MD, PhD[d]

From the Departments of [a]Pediatrics; [b]Internal Medicine, The Ohio State University College of Medicine; [c]Section of Pulmonary Medicine, Nationwide Children's Hospital; Departments of [d]Surgery; [e]Anesthesiology, The Ohio State University College of Medicine; and the [f]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, Ohio.

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BACKGROUND: No restrictions exist for allocating donor lungs according to age in the United States.
METHODS: A retrospective cohort study was performed of lung transplant recipients from 1987 to 2013 through a query of the United Network for Organ Sharing (UNOS) thoracic database. Age thresholds used were recipients (R) aged 60 years (R60 group) and 65 years (R65 group) and donors aged 50 years; each sub-group was analyzed, totaling 8 groups.
RESULTS: Of 23,905 lung transplants, 23,704 were used for Kaplan-Meier analysis, 8,851 for multivariate Cox, and 3,206 for the R60 group and 3,212 for the R65 group propensity score-matching analysis. Kaplan-Meier analysis with log-rank test statistic indicated significant differences across binary measure of donor age with a threshold of 60 years (log-rank test: chi-square$_1$ = 12.9558, $p = 0.0003$) and 65 years (log-rank test: chi-square$_1$ = 15.5053, $p = 0.0001$). Multivariate Cox models demonstrated that donors aged < 50 years and ≥ 50 years significantly reduced the risk for death for the R60 group, whereas only donors aged < 50 years decreased risk for death for the R65 group (hazard ratio [HR], 0.730; 95% confidence interval [CI], 0.623–0.856; $p < 0.001$) after lung transplant. Propensity score-matching analysis showed donors aged ≥ 50 years increased the risk for death of recipients aged < 60 years (HR, 1.314; 95% CI, 1.065–1.621; $p = 0.011$) and < 65 years (HR, 1.198; 95% CI, 1.089–1.319, $p < 0.001$), whereas donors aged ≥ 50 years did not increase the risk for death for recipients aged ≥ 60 years (HR, 1.056; 95% CI, 0.869–1.285; $p = 0.583$) and ≥ 65 years (HR, 0.938; 95% CI, 0.705, 1.249, $p = 0.662$).
CONCLUSIONS: Older donor lungs did not negatively affect survival in older recipients but limited outcomes in younger recipients.
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With an aging population, patients on organ transplant waiting lists and patients donating organs are growing older.[1] Currently, the number of patients aged >65 years undergoing lung transplantation (LTx) is on the rise, coinciding with an increase in the age of donor lung allografts.[2] In relation to younger donor organs, a higher proportion of organs from older donors are discarded and not used for LTx.[1,2]

Lung allografts from donors aged ≥ 60 years are associated with a lower 10-year survival, with bronchiolitis obliterans syndrome (BOS) being the predominant cause of death.[3] A recent study found that 1-year rates of graft failure were increased in recipients of donor lungs aged

Reprint requests: Don Hayes, Jr., MD, MS, The Ohio State University, Nationwide Children's Hospital, 700 Children's Dr, Columbus, OH 43205. Telephone: +614-722-3425. Fax: +614-722-3426.
E-mail address: hayes.705@osu.edu

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≥65 years (hazard ratio [HR], 2.15; 95% confidence interval [CI], 1.47–3.15).[4]

The effect of older donor age on transplantation varies by organ, with limited data examining the effect of age between donor and recipients after LTx. The current medical literature studying the effects of younger recipients receiving older donor organs and older recipients receiving younger organs in LTx is limited, with the need for further study. Using an available database in the United States, we sought to assess the influence of donor-recipient age matching on outcomes after LTx, specifically with the use of older donor lungs.

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 (STAR) Database administered by United Network for Organ Sharing (UNOS) since 1987.[5] The study was approved by The Ohio State University Wexner Medical Center Institutional Review Board (IRB #2012H0306), with a waiver of the need for individual consent. The UNOS/OPTN thoracic database was queried for all lung transplants from January 1, 1987, to September 6, 2013.

Statistical methods

All analyses were performed using Stata/MP 13.0 software (StataCorp LP, College Station, TX). For all analyses, a *p*-value of ≤0.05 was considered statistically significant. Descriptive statistics for continuous variables are presented as means and standard deviations, and descriptive statistics for categoric variables are presented as proportions. To assess the differences regarding age in our analysis, histograms were used to identify mean age for the study groups. On the basis of frequency in the histograms, thresholds of 60 and 65 years were identified for recipients (R) and 50 years for the donors (D). Therefore, the groups analyzed included $R < 60$ $D < 50$, $R < 60$ $D \geq 50$, $R \geq 60$ $D < 50$, $R \geq 60$ $D \geq 50$, $R < 65$ $D < 50$, $R < 65$ $D \geq 50$, $R \geq 65$ $D < 50$, and $R \geq 65$ $D \geq 50$.

Survival duration was analyzed from the date of the transplant until the date of death or censoring. Kaplan-Meier survival curves were fitted separately to each of the categories defined by recipient and donor age, and a log-rank test was performed to assess differences across the survival curves. A Cox proportional hazards model was used to adjust for potential confounders, which included donor and recipient gender, donor and recipient race, type of transplant (double), pulmonary hypertension (PH), recipient and donor cytomegalovirus (CMV) status, major infection, creatinine, body mass index (BMI), and ischemic time. We defined PH as a mean pulmonary artery pressure ≥35 mm Hg based on an unpublished analysis by our group identifying that this level of PH significant affects mortality of several groups of patients with advanced lung disease undergoing LTx.

To further adjust for baseline differences between recipients with $D < 50$ and with $D \geq 50$, a propensity analysis was performed separately for the $R < 60$ and $R \geq 60$ and $R < 65$ and $R \geq 65$ groups. The propensity of having $D \geq 50$ was calculated separately in each of these groups as a logit function of the covariates included in the Cox analysis. The matching algorithm used 1:1 nearest-neighbor matching (without replacement) on the logit of the propensity score, with a caliper width equal to 0.2 standard deviations of the logit of the propensity score. Cox proportional hazards regression stratified on the matched pairs was used to assess the HR associated with $D \geq 50$ in each subgroup defined by recipient age ($R < 60$ or $R \geq 60$, $R < 65$ or $R \geq 65$).

Results

Study population

Figure 1 presents inclusion and exclusion criteria for our study. Of the 136,498 organ transplant candidates, 23,905 were first-time LTx recipients aged >18 years with a known first transplant date from a cadaveric donor and were not a duplicate entry. Further exclusion included identical waiting list entry and exit dates for Kaplan-Meier survival curve

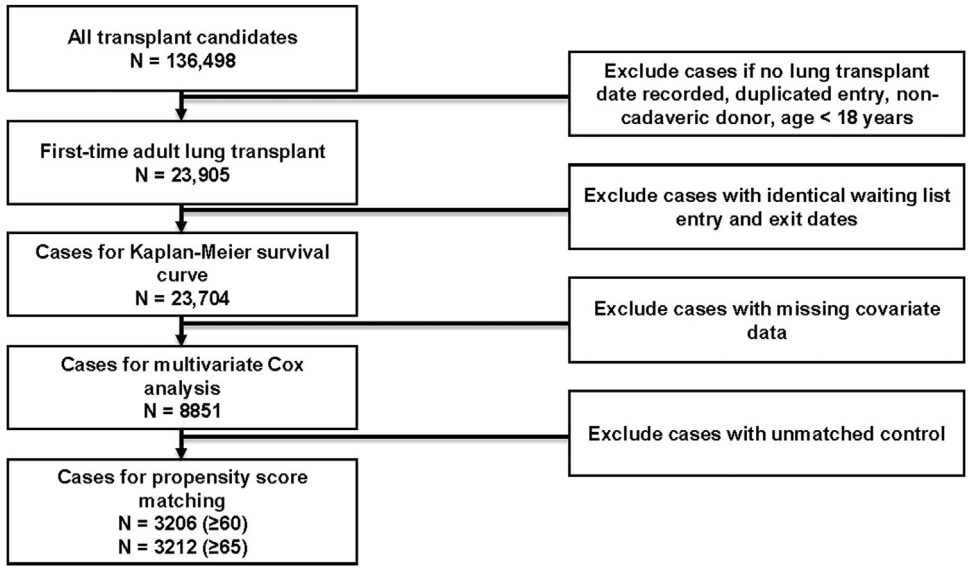

Figure 1 Patient inclusion and exclusion criteria for Kaplan-Meier survival analysis, multivariate Cox analysis, and propensity score matching.

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