Influence of Donor Smoking on Midterm Outcomes After Lung Transplantation

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Background. **Lung transplantation (LTx) is significantly limited by donor organ shortage. Donor smoking history of more than 20 pack-years is considered an extended donor criterion. In this study, we retrospectively evaluated impact of donor smoking history and extent of smoking on midterm outcome after LTx.**

Methods. **In all, 237 LTx were performed in our institution between 2007 and 2012. Patients were divided into three groups, receiving lungs from 53% nonsmoking donors, 29% smoking donors with fewer than 20 pack-years, and 18% heavy smokers with more than 20 pack-years.**

Results. **Preoperative donor and recipient characteristics among the groups were comparable. However, donors from the heavy smokers group were significantly older ($p < 0.001$). The overall presence of abnormal histology (inflammation or metaplasia) in donor main bronchi samples increased with the extent of smoking but did not reach statistical significance ($p = 0.211$). Although metaplasia was found in significantly more donors from the heavy smokers group ($p = 0.037$), this did not translate into inferior outcomes for the recipients. There were no statistically significant differences in PaO_2/FiO_2 ratio after LTx, duration of mechanical ventilation ($p = 0.136$), intensive care unit stay ($p = 0.133$), and total postoperative hospital stay ($p = 0.322$). One-year and three-year survival were comparable across all three groups (log rank $p = 0.151$). Prevalence of bronchiolitis obliterans syndrome ($p = 0.616$), as well as bronchiolitis obliterans syndrome free survival ($p = 0.898$) after LTx were also comparable.**

Conclusions. **In our experience, history and extent of donor smoking do not significantly affect early and midterm outcomes after LTx. Although this finding does not obviate the need for longer-term observation, donor lungs from even heavy smokers may not per se contraindicate LTx and may provide a valuable avenue for expanding donor organ availability.**

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Lung transplantation (LTx) is a life-saving therapy for patients with end-stage lung disease, but shortage of organ donors results in significant waiting list mortality. The UK Transplant Registry data show that for patients listed for a lung transplant, only 20% receive transplants within 6 months, rising to 51% after 3 years, by which time 30% have died waiting for a transplant [1]. Because of injuries to the lung during the process of brain death and complications related to the intensive care unit (ICU), only 17% of actual donors in the United States and 15% in the United Kingdom donate lungs [2, 3]. To overcome this donor shortage several techniques such as optimization of donor management, use of extended criteria donors, cardiocirculatory arrest donors, as well as ex-vivo lung perfusion are being utilized [4–7]. Maximizing donor selection is an important strategy to reducing waiting list mortality.

Donor smoking history is one of the major guideline variables for donor selection, and a previously accepted criterion for an ideal donor is a smoking history of less than 20 pack-years, with a smoking history of more than 20 pack-years putting the donor into the category of an extended donor [8]. Given the prevalence of smoking in the general population, and consequently in the organ donation pool, a policy of refusal to use lung allografts from smokers would have a profound impact on the number of available organs [9]. Conversely, the risk that a positive smoking history in lung donors could adversely affect transplant outcome causes concern [10]. In an attempt to address this pertinent issue, we collected and analyzed patient and donor characteristics, as well as outcome data, for all lung transplantations performed at our center over a 6-year period and investigated the association between donor smoking history and several measures of outcome.

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Material and Methods

The Institutional Review Board at our center approved this study and waived the need for individual patient consent.

The study design was a retrospective review of the prospectively collected data. A total of 237 LTx were performed at Harefield Hospital between January 2007 and September 2012. Recipients were divided into three groups depending on smoking history of the donors from whom they received organs: 123 (53%) nonsmoking (NS) donors, 68 (29%) smoking (S) donors who had smoked less than 20 pack-years, and 41 (18%) heavily smoking (HS) donors with a smoking history of more than 20 pack-years. One pack-year was defined as 20 cigarettes (one pack) smoked per day for 1 year. Five patients were excluded owing to unknown donor smoking history, leaving 232 patients for further analysis.

Endpoints of the Study

Primary endpoints of the study were overall survival after lung transplantation and survival free of bronchiolitis obliterans syndrome (BOS). Secondary endpoints included postoperative recipient characteristics: paO_2/FiO_2 ratio at the end of the transplant and 24, 48, and 72 hours after transplant, duration of mechanical ventilation, intensive care unit (ICU) and total hospital stay, and need for postoperative use of extracorporeal membrane oxygenation.

Organ Assessment and Organ Procurement Protocol

Donor organ assessment performed at donor hospitals included radiologic assessment, fiberoptic bronchoscopy, gross organ inspection and palpation, assessment of compliance using deflation test, and selective blood gas analysis from each pulmonary vein. The final decision of proceeding with organ procurement and transplantation was taken by the implanting surgeon. The standard preservation solution used was low potassium dextran (Perfadex; Medisan, Uppsala, Sweden) solution augmented with CaCl2, 3.6% tromethamine (THAM; Hospira, Lake Forest, IL), and epoprostenol sodium 2.5 mL/L. For donation after brain death, 4 L of the solution was usually administered antegradely through a Medtronic (Minneapolis, MN) 24F single-stage venous cannula and 1 L retrogradely through a Medtronic 15F retrograde cannula with self-inflating balloon. For donation after cardiac death (DCD), 3 L of pneumoplegia was administered antegrade and 2 L retrograde. During the pulmonary artery flush, a flushing pressure between 10 and 15 mm Hg was maintained. Once the organs were removed from the chest, they were inspected and then packed for storage on ice and transported half inflated with FiO_2 0.5. Samples of donor main bronchi were taken during organ implantation and sent for histopathology assessment. Also, intrabronchial swabs were collected for microbiological analysis. The total ischemic time was defined as the time between cardiac arrest in DCD donors or aortic cross-clamp in donation after brain death donors and reperfusion of the second implanted lung.

Detailed donor data, such as demographic variables, cause of death, current clinical status, laboratory investigations, and social and medical history were analyzed. The information about donor smoking habits and estimate of pack-year consumption were obtained from the general practitioner or donor's next of kin. Demographics and perioperative recipient data as well as midterm outcome were compared. BOS was diagnosed when posttransplant fraction of expired volume in 1 s (FEV_1), measured on a regular basis after the transplant, permanently dropped more than 20% of the best FEV_1 achieved after LTx.

Statistical Analysis

Data were obtained from cardiothoracic donor information forms and recipient chart review. Statistical analysis was performed using IBM SPSS Statistics version 21 software (SPSS, Chicago, IL). The data are presented as continuous or categorical variables. Continuous data were evaluated for normality using the one-sample Kolmogorov-Smirnov test, and are expressed as the mean $\pm$ SD in cases of normally distributed variables or median (interquartile range) in cases of nonnormally distributed variables. Categorical data are expressed as total numbers and percentages. Intergroup comparisons were performed using either one-way analysis of variance or the Kruskal-Wallis test for normal and nonnormal continuous variables, respectively. Pearson's χ^2 or Fisher's exact tests were used for categorical data depending on the minimum expected count in each cross tabulation. A p value less than 0.05 was considered statistically significant. Kaplan-Meier actuarial survival curves were generated to analyze post-LTx survival and survival free of BOS.

Results

Of 237 LTx performed between January 2007 and September 2012, 214 (90.3%) were double-lung transplantations and 23 (9.7%) were single-lung transplantations. Lungs were retrieved from 237 donors who met the assessment criteria for lung transplantation. In 45 cases (19%), lungs were retrieved from DCD donors. Organ procurement was performed by six designated lung transplant centers in the United Kingdom, including ours, within the specified geographic region of each center. Overall, 147 organs (60.03%) were procured by our retrieval team whereas 90 organs (37.97%) were procured by other five centers and sent to Harefield Hospital for further lung transplantation. The lungs were matched to the recipients according to blood group, height, total lung capacity, time on the waiting list, and clinical status of the recipient at the time of transplantation.

After exclusion of patients who received transplants using organs from donors with unknown smoking history (n = 5, 2.11%), donors from the NS, S, and HS groups had comparable baseline characteristics, except for significantly higher donor age in the HS group: 47.93 $\pm$ 7.03 years, compared with 37.75 $\pm$ 11.55 years in the S group and 42.46 $\pm$ 13.91 years in the NS group ($p < 0.001$). As presented in Table 1, there were no statistically significant