Examining ABO Compatible Donors in Double Lung Transplants During the Era of Lung Allocation Score

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Background. **The short-term and long-term effect of using ABO compatible donors in the era of lung allocation score is unknown. This study determined if carefully selected ABO compatible donors could be used in double lung transplantation (DLT) with good outcomes.**

Methods. **The United Network for Organ Sharing database was retrospectively reviewed for adult DLT from May 2005 to December 2011.**

Results. **Of 6,655 double lung transplants, 493 (7.4%) were with ABO compatible donors and 6,162 (92.6%) were with ABO identical donors. In multivariate analysis, use of ABO compatible donors was not associated with mortality at 30 days (HR, 1.16; 95% CI, 0.76 to 1.79, $p = 0.49$), 1 year (HR, 1.10; 95% CI, 0.86 to 1.42, $p = 0.46$), and 5 years (HR, 1.06; 95% CI, 0.83 to 1.34, $p = 0.65$). Variables associated with mortality at 5 years were donor female sex, donor age 60 years or greater, prolonged ischemic time, increasing recipient creatinine, recipient age, race mismatch, and mechanical ventilation or extracorporeal membrane oxygenation as a bridge to transplantation. Length of stay was longer in the ABO compatible group (30.9 vs 25.9 days, $p = 0.001$). Acute rejection episodes on index hospitalization (8.8 vs. 8.9%, $p = 1.00$), peak posttransplant forced expiratory volume in 1 second (FEV_1) (82.7 vs 79.7%, $p = 0.053$), and decrement in FEV_1 over time were not different ($p = 0.13$). Freedom from bronchiolitis obliterans syndrome was similar (1,475 vs 1,454 days, $p = 0.17$).**

Conclusions. **The use of ABO compatible donors in the era of lung allocation score was not associated with short-term or long-term mortality and resulted in equivalent posttransplant lung function. A DLT with carefully selected ABO compatible donors can result in excellent outcomes.**

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Lung transplantation remains the gold standard for select patients with end-stage lung disease refractory to medical therapy [1, 2]. While the institution of lung allocation score (LAS) in May 2005 has shortened time to receiving a lung transplant and decreased the risk of death on the waiting list [3–5], there continues to be a critical shortage of organ donors [2]. This shortage of organ donors has led to the liberalization of selection criteria for lung transplant donors [6–13]. The ABO identical donors are thought to be preferable to ABO compatible donors and the current United Network for Organ Sharing lung allocation protocol gives priority to ABO identical matches [14]. While ABO compatible donors are being used in double lung transplantation [10], the long-term effects of using such donors are not known. Single institutional studies have shown that use of ABO compatible donors is safe; however, these studies have been limited by short follow-up time and small sample size [15, 16]. In addition, these studies were all performed prior to the era of LAS. The goal of this study was to use a large, national database to determine how using ABO compatible donors affects morbidity and mortality in double lung transplantation. We hypothesized that double lung transplantation with ABO compatible donors could result in good outcomes.

Patients and Methods

Data Source

After approval from the Temple University Institutional Review Board (IRB), public-use Standard Transplant Analysis and Research data files were obtained from the United Network for Organ Sharing (UNOS) registry. All double lung transplants performed in the United States in adults over the age of 18 as reported to UNOS were

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Abbreviations and Acronyms

BMI = body mass index
BOS = bronchiolitis obliterans syndrome
COPD = chronic obstructive pulmonary disease
ECMO = extracorporeal membrane oxygenation
FEV_1 = forced expiratory volume in 1 second
HLA = human leukocyte antigen
INO = inhaled nitric oxide
IPF = idiopathic pulmonary fibrosis
IRB = Institutional Review Board
LAS = lung allocation score
PRA = plasma reactive antigen panel
UNOS = united network for organ sharing

examined from May 2005 to December 2011. The analysis was started in May of 2005 as this corresponded to the institution of LAS. Recipients of ABO compatible donors were compared with those of ABO identical donors. The primary endpoint measured was risk-adjusted all cause mortality. Secondary endpoints included length of stay, freedom from bronchiolitis obliterans syndrome (BOS), peak posttransplant 1-second forced expiratory volume (FEV_1), and mean decrement of posttransplant FEV_1.

Statistical Analysis

The Student t test and χ^2 test were used to examine continuous and categoric variables. Continuous variables are presented as mean ± SD or median (range) and categoric variables are reported as percentages of the total number of data points available for that field. Survival curves were generated using the Kaplan-Meier method and compared with the long-rank test. Cox proportional regression analysis was developed in 2 steps. First, covariates were run in a univariate analysis as predictors of mortality. All covariates analyzed are shown in Tables 1 to 4. Next, covariates with a p value less than 0.20 were entered simultaneously as a multivariate Cox model. In addition, we tested 2-way interactions between ABO compatible donors and recipient age, recipient sex, donor age, donor sex, and ischemic time. Because none of these interactions were significant, they were not retained in the final model. Covariates missing greater than 15% of data in the registry were excluded from the analysis. Survival was determined using all cause mortality. This multivariate analysis was performed at 30 days, 1 year, and 5 years posttransplantation. Freedom from BOS was analyzed by Kaplan-Meier analysis and compared with the log-rank test. A linear mixed-effects model with a treatment by time interaction term was used to evaluate between-group differences in posttransplant FEV_1. Data were analyzed using SAS statistical software version 9.2 (SAS Institute, Cary, NC).

Results

There were 6,655 total adult double lung transplants during the study period as reported to UNOS. Of these, 493 (7.4%) were carried out using ABO compatible donors. Mean follow-up in the ABO identical and compatible cohorts were 734.3 and 775.4 days.

Recipient Characteristics

Recipients of ABO compatible donors were more likely to have a primary diagnosis of emphysema or chronic obstructive pulmonary disease (COPD) as seen in Table 1. Recipients of ABO identical donors were more likely to have a primary diagnosis of idiopathic pulmonary fibrosis (IPF). The 2 groups were not different with respect to a primary diagnosis of cystic fibrosis, congenital disease, primary pulmonary hypertension, or retransplantation or graft failure.

Baseline clinical characteristics are shown in Table 2. Recipients of ABO compatible donors had lower LAS and higher forced vital capacity. There was no difference between the 2 recipient groups with respect to age, sex, ethnicity, body mass index, FEV_1, cardiac output, pulmonary vascular resistance, baseline creatinine, or the requirement of inhaled nitric oxide, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) as a bridge to transplantation.

Donor Characteristics

A comparison of donor characteristics is shown in Table 3. The ABO compatible donors had higher body mass index. The 2 groups were similar with respect to donor age, sex, history of cancer, history of heavy

Table 1. Primary Diagnoses of All Patients

Primary Diagnoses	ABO Identical (n = 6,162)	ABO Compatible (n = 493)	p Value
Idiopathic pulmonary Fibrosis	1,622 (26.3)	103 (20.9)	0.001
Emphysema/chronic Obstructive pulmonary disease	1,455 (23.6)	173 (35.1)	<0.001
Cystic fibrosis	1,154 (18.7)	85 (17.2)	0.45
Congenital disease	17 (0.3)	1 (0.2)	0.89
Primary pulmonary Hypertension	155 (2.5)	15 (3.0)	0.53
Alpha-1 antitrypsin Deficiency	200 (3.3)	20 (4.1)	0.40
Retransplant/graft failure	207 (3.4)	17 (3.5)	1.00
Other	1,352 (21.9)	79 (16.0)	0.003