The Effect of Donor Age on Survival after Lung Transplantation

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Abstract

Background: Historically, donor age above 55 years has been considered to be a relative contraindication for organ transplantation. The shortage of organs for transplantation has led to the expansion of the donor pool by accepting older donors.

Objectives: To compare the 1 year follow-up in patients after lung transplantation from older donors (> 50 years old) and in patients after transplantation from younger donors (⩽ 50 years).

Methods: The study group comprised all adult patients who underwent lung transplantation at the Rabin Medical Center between May 1997 and August 2001. Donors were classified into two groups according to their age: ⩽ 50 years (n = 20) and > 50 years (n = 9). Survival, number and total days of hospitalization, development of bronchiolitis obliterans syndrome, and pulmonary function tests, were examined 1 year after transplantation.

Results: We performed 29 lung transplantations in our center during the observed period. Donor age had no statistically significant impact on 1 year survival after lung transplantation. There was no statistically significant effect on lung function parameters, the incidence of hospitalization or the incidence of bronchiolitis obliterans between both donor age groups at 1 year after transplantation.

Conclusions: Donor age did not influence survival or important secondary end-points 1 year after lung transplantation. By liberalizing donor criteria of age up to 65 years, we can expand the donor pool, while assessing other possible mechanisms to increase donor availability.

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The most important limitation in lung transplantation both worldwide and in Israel is donor availability. In the past 4 years only 60 lung transplantations (about 10 cases per million) were performed in Israel. The willingness to offer organs for transplantation varies among countries: 44–49% in Israel, 50% in Germany, and up to 80% in Belgium and Scandinavia [1]. Although lung transplantation has clearly become a therapeutic option for patients with end-stage pulmonary disease, the number of available donors currently limits this option [2]. The problem of lung transplantation is even greater than that of cardiac or liver transplantation, since only 15–20% of multiple organ donors have functional lungs for transplantation by the current criteria [3]. Thus, many centers have attempted to expand the donor pool by using lungs from older donors. We report here our experience with such donors.

Patients and Methods

All adult patients undergoing lung transplantation at the Rabin Medical Center between May 1997 and August 2001 were included in this study. Donors were classified into two groups: donor age ⩽ 50 years and > 50 years. Patient survival was examined after 1 year of transplantation. Also examined in both groups 12 months after transplantation were secondary end-points, which included number and total days of hospitalization, development of bronchiolitis obliterans syndrome, and pulmonary function (forced expiratory pressure at 1 second, forced vital capacity, and forced expiratory flow 50%). Immunosuppressive therapy after transplantation was a combination of cyclosporine, azathioprine and prednisone until November 1998, and thereafter tacrolimus, mycophenolate mofetil and prednisone. Procurement of the lung to be transplanted was in UW solute

Statistical analysis

Mean ± standard deviations were calculated for continuous variables. Pearson correlation coefficients (r) and their significance (P) were calculated between the variables. In order to analyze statistically significant differences in mean continuous parameters (i.e., FVC, FEV1 etc.) between the two groups of patients, Student's t-test was used. Fisher's exact test was used to analyze statistically significant relationships in the distribution of categorical date (i.e., death) between both groups of patients. P values ⩽ 0.05 were considered statistically significant.

Results

Demographics

A total of 29 lung transplantations were performed at the Rabin Medical Center (Beilinson Campus) during the observed period: 4 heart-lung, 3 double lungs, and 22 single transplantations. Donors were separated into two groups according to their age: ⩽ 50 years (n=20) and > 50 years (n=9). Demographic data, including donor age and smoking status, recipient age, gender, diagnosis, transplantation type and immunosuppressive therapy, are shown in Table 1. Except for donor age, the demographic characteristics in both groups were similar.

Survival

Donor age had no statistically significant impact on 1 year survival after lung transplantation. Fourteen of the 20 transplanted patients (70%) who received lungs from donors younger than 50 years, and 7 of the 9 (78%) who received lungs from older donors, survived.

FVC = forced vital capacity
FEV1 = forced expiratory flow in 1 second

Table 1. Demographic characteristics stratified by donor age (n = 29)

	Donor age ⩽ 50 years (n=20)	Donor age > 50 years (n=9)
Donor age, mean ± SD (range)	29.1±9.6 (20–45)	56.0±4.6 (51–62)
Donor smoker, n (%)	8 (40%)	3 (33%)
Recipient diagnosis:		
Emphysema	10	5
Pulmonary fibrosis	6	3
Cystic fibrosis	2	1
Pulmonary hypertension	2	0
Recipient age, mean ± SD (range)	54.1±10.2 (30–65)	49.8±15.8 (15–64)
Recipient gender (M/F)	16/4	7/2
Transplantation type		
Single lung	16	6
Double lung	2	1
Heart-lung	2	2
Immunosuppressive therapy:		
Cy/AZ/P	5	3
FK/MMF/P	15	6

Cy = cyclosporine, AZ = azathioprine, P = prednisone, FK = tacrolimus, MMF = mycophenolate mofetyl

Table 2. Donor age groups: analysis of survival and secondary end-points

	Donor age ⩽ 50 years (n=20)	Donor age > 50 years (n=9)	*P*
Alive 1 yr after transplantation	14/20	7/9	1.00
No. of hospitalizations (mean ± SD)	1.0±1.2	3.1±3.0	0.067
Total days of hospitalization	7.4±10.5	22.8±30.8	0.175
Bronchiolitis obliterans	1	2	0.220
Lung function* (% predicted):			
FVC	2.34±0.68 (81.3%)	2.17±0.51 (62.4%)	0.544
FEV1	1.69±0.67 (72.2%)	1.54±0.43 (62.4%)	0.552
FEF 50%	0.78±0.65 (30.5%)	0.64±0.74 (23.2%)	0.638

* Lung function is presented as absolute values in ml, mean ± SD and as (mean of percentages of predicted values)

FEF = forced expiratory flow.

Secondary end-points

The impact of donor age on secondary end-points was evaluated. There was no statistically significant effect on the incidence of hospitalization, total days of hospitalization, lung function parameters, and the incidence of bronchiolitis obliterans syndrome between both donor age groups during the first year following transplantation [Table 2].

Discussion

Our results showed no significant difference in 1 year survival and secondary end-points between the recipients of lungs from older donors and those who received lungs from younger donors. Specifically, the two groups did not significantly differ in the number of hospitalization days, total days of hospitalization, bronchiolitis obliterans syndrome, and lung function parameters. Nevertheless, we observed a slightly decreased pulmonary function (FEV1 1.54 ± 0.43 vs. 1.69 ± 0.67, respectively) and a slightly increased number of hospitalizations at 1 year (1.0 ± 1.2 vs. 3.1 ± 3.0 hospitalizations and 7.4 ± 10.5 vs. 22.8 ± 30.8 days of hospitalization during the first year, respectively) in the recipients of lungs from older donors as compared with those from younger donors, although this difference did not reach statistical significance. These findings may suggest a slight loss of lung function in this group. Nevertheless, survival in the group of patients receiving lungs from older donors was slightly better than in the group receiving lungs from younger donors.

The continual shortage of solid organs for transplantation led to expansion of the donor pool by accepting older donors. A retrospective cohort analysis of 1,800 lung transplant recipients operated in the United States between April 1993 and March 1996, with complete 2 year follow-up, assessed the influence of donor age and ischemic time on survival and other secondary end-points [4]. The secondary end-points were: hospitalization for rejection, bronchiolitis obliterans syndrome, FEV1, bronchial stricture, and hospitalization for infection. It was found that donor age and donor ischemic time did not independently influence survival or secondary end-points after lung transplantation. However, intermediate-term survival was affected by the use of older donors when combined with prolonged ischemic time. In another study using marginal lung donors, Sundaresan and co-workers [3,5] compared the results of standard acceptable pulmonary donors and donors who did not meet the acceptability criteria, which included age < 50 years, smoking < 20 pack-years and PaO_2 > 300 mmHg. There was no significant difference in 30 day mortality between both groups. Sommers et al. [6] demonstrated a correlation between donor age and early graft dysfunction within the first hours after transplantation but not at 1 year after transplantation.

The use of older donors in cardiac transplantation was studied by Loebe et al. [7]. They analyzed postoperative mortality, cumulative survival rates, cardiac dependent morbidity, changes in the left/right ventricular ejection fraction, as well as absence of both cytomegalovirus infection and acute rejection episode according to the donor age. Donor age was divided into three groups: < 35 years, 35–50 years and > 50 years. They did not find a significant difference in the mid-term follow-up between patients who received hearts from 35–50 year old donors and those who received hearts from donors > 50 years. In another study the same group analyzed the medium-term follow-up of patients who received a heart from donors older than 63 years as compared to patients who received younger hearts [8]. They found a significant increase in long-term cardiac morbidity due to more focal coronary stenosis and absence of cytomegalovirus in patients who received hearts from older donors, but did not find any significant differences in the long-term survival between patients who received hearts from donors less than 63 years of age and those who received hearts from donors older than 63 years.

The use of older donors enabled us to increase the number of lung transplantations performed in our hospital in the past 4 years without compromising the outcome of transplant recipients.

Although we advocate liberalization of the donor age and use of older donors for lung transplantation, careful clinical judgment is essential at the time of procurement. In addition to the careful evaluation of all donor criteria, consideration must also be given to the potential donor's underlying disease, concomitant disease(s), smoking status, ischemic time, and time on a respirator [9].

In conclusion, on the basis of our data and previous published data showing lack of influence of donor age on transplantation outcome and survival, clinicians should increase their efforts in recruiting potential lung donors without taking the donor's age as an absolute limiting factor. This change could lead to the potential donation of more organs and thus transplantation of a greater number of patients. This may lessen the gap between the number of patients waiting for lung transplantation and the number who undergo transplantation, and will likely result in a future decrease in the number of deaths of people on the waiting list.

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