The Effect of Gender Combinations on Outcome in Human Lung Transplantation: The International Society of Heart and Lung Transplantation Registry Experience

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Background: In the current practice of lung transplantation, donor and recipient genders are neither directly considered nor matched.

Methods: We analyzed the potential effect of gender combinations on survival in 9,651 lung transplant recipients in the International Society of Heart and Lung Transplantation Registry (ISHLT) Registry. We compared the risk of overall and 90-day mortality by using statistical models that accounted for confounding variables.

Results: A Kaplan-Meier survival analysis revealed a significant difference of survival among gender combinations (log rank, $p = 0.0009$). The unadjusted odds ratio (OR) of 90-day mortality was significantly higher in female (F) donors to male (M) recipients (OR, 1.58; 95% confidence interval (CI), 1.22–2.04; $p < 0.001$) and lower in F to F (OR, 0.742; 95% CI, 0.61–0.90; $p = 0.004$) compared with the reference category of M to M. After adjusting for size mismatch and diagnosis in the multivariate logistic regression model, the OR of F to M was still statistically significant (F to M OR, 1.52l; 95% CI, 1.04–2.20; $p = 0.028$; F to F OR, 0.67; 95% CI, 0.53–0.91; $p = 0.008$) for 90-day mortality. A Cox proportional hazards analysis for overall survival also showed a significantly higher hazard ratio of 1.12 in F to M (95% CI, 1.01–1.23) and a lower hazard ratio of 0.92 in F to F (95% CI, 0.87–0.98).

Conclusion: ISHLT Lung Transplant Registry data demonstrated a significant risk for F to M. Interestingly, F to F appears to be potentially beneficial in lung transplantation. Gender combinations do appear to significantly impact outcome after lung transplantation. J Heart Lung Transplant 2006;25:634–7.

Since the first reported long-term survival case in 1983,[1] lung transplantation has achieved remarkable progress and is used worldwide in the treatment of selected patients with end-stage lung disease. Despite the careful donor selection, however, 5-year patient survival is limited to 45%.[2] Further efforts for more effective patient selection are therefore needed in the search for better short-term and long-term survival of lung transplant recipients.

In the current practice of lung transplantation, many issues are considered in donor lung evaluation. As donor and recipient factors, ABO compatibilities, cytomegalovirus serology, and size matching are taken into consideration; however, donor and recipient gender are neither directly considered nor matched. A few reports have focused on gender matching in lung transplantation but with limited sample sizes because of single-center analyses.[3,4]

The present study analyzed the effects of gender combinations on recipient survival by using the data of 9,651 cases of lung transplantation in the International Society of Heart and Lung Transplantation Registry (ISHLT) Registry. Variables among gender combinations such as lung size mismatch and recipient diagnosis were also considered as confounding factors in multivariate regression analyses.

METHODS

Patients

The data relating to 9,651 cases of lung transplantation from January 1, 1995 through June 30, 2002 in the ISHLT Registry database were analyzed. Cases were distributed into 4 groups according to recipient and donor gender: male donor to male recipient (M to M, $n = 3,855$), male donor to female recipient (M to F, $n =$

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Table 1. Baseline Patient Characteristics of the ISHLT Registry*

	Overall $n = 9651$ (%)	M to F $n = 1867$ (%)	F to M $n = 1076$ (%)	F to F $n = 2853$ (%)	M to M $n = 3855$ (%)	p
Transplant procedure						<0.0001
Single	5084 (52.7)	1085 (41.8)	490 (45.5)	1424 (49.9)	2084 (54.1)	
Bilateral	4567 (47.3)	781 (58.2)	586 (54.5)	1429 (50.0)	1771 (45.9)	
Recipient diagnosis						<0.0001
IPF	1554 (16.1)	223 (11.9)	259 (24.1)	357 (12.5)	715 (18.6)	
CF	1374 (14.2)	223 (11.9)	220 (20.5)	383 (13.4)	548 (14.2)	
α-1	853 (8.8)	131 (7.0)	71 (6.6)	205 (7.2)	446 (11.6)	
PPH	402 (4.1)	93 (5.0)	38 (3.5)	169 (5.9)	102 (2.7)	
COPD	3625 (37.6)	848 (45.4)	303 (28.2)	1061 (37.2)	1413 (36.7)	
Others	1843 (19.1)	349 (18.7)	185 (17.2)	678 (23.8)	631 (16.4)	
ABO blood type compatibility						

1,867), female donor to female recipient (F to F, $n = 2,853$), and female donor to male recipient (F to M, $n = 1,076$).

Survival Analysis

Baseline characteristics of patients were compared by analysis of variance for continuous variables and chi-square analysis for categoric variables. The predicted total lung capacity (TLC) of donors and recipients was calculated from height and age on transplantation as follows:

Male: predicted TLC (L) = (0.094 × height in cm) − (0.015 × age in years) − 9.167.

Female: predicted TLC (L) = (0.079 × height in cm) − (0.008 × age in years) − 7.49.

Survival rates were calculated by the Kaplan-Meier method and compared with the log-rank test.

Potential confounding factors that could affect the interpretation of the gender-combination effect on survival were considered for adjustment in multivariate logistic regression analysis and Cox proportional hazard analysis. The following variables were included in the formula: donor/recipient predicted TLC ratio, donor/recipient ABO blood type compatibility, recipient diagnosis, recipient age, recipient body mass index (BMI), donor age, and lung transplantation procedure.

The ratio of donor and recipient predicted TLC was categorized into 3 groups: upper and lower 25th percentile and middle 50%. Recipient diagnosis was categorized into 5 groups: (1) chronic obstructive pulmonary disease (COPD), (2) idiopathic pulmonary fibrosis, (3) α-1 anti-trypsin deficiency emphysema, (4) cystic fibrosis, and (5) primary pulmonary hypertension. Lung transplantation procedure was used as a categoric value (i.e., single or bilateral). ABO blood type compatibility was categorized into 2 groups: identical and non-identical. Recipient age, recipient BMI, and donor age were used as continuous variables after confirmation of their log-linearity in odds ratio (logistic regression analysis) or hazard proportionality (Cox analysis). JMP 5.0 software (SAS Institute Inc, Cary, NC) for Windows (Microsoft, Redmond, WA) was used for all data analysis. Statistical significance was set at $p < 0.05$.

RESULTS

Unadjusted Analysis of the ISHLT Registry

Baseline characteristics of patients from the ISHLT Registry are listed in Table 1. Significant differences were found among the gender combinations in each variable.

Survival curves of each gender combination are depicted using standard Kaplan-Meier actuarial techniques for estimation of survival probabilities (Figure 1). The log-rank test showed a significant difference of survival among combinations ($p = 0.0009$). The F to M survival curve separated from other curves within the first 3

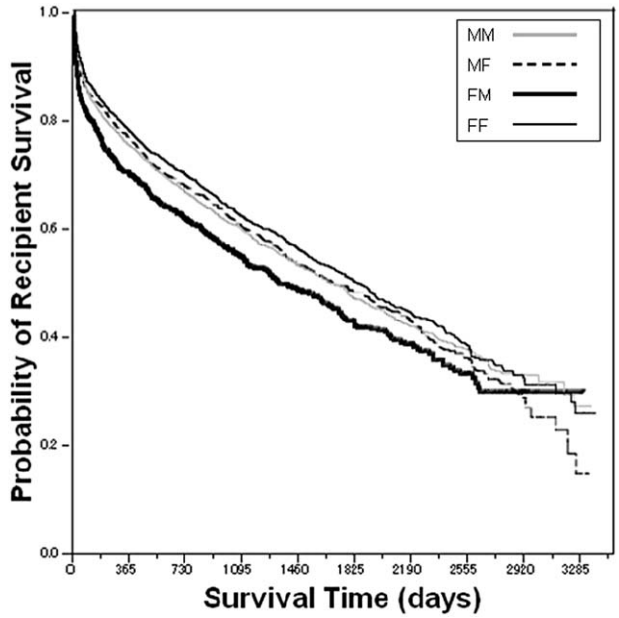

Figure 1. Kaplan-Meier estimate of survival for the ISHLT Registry. Log-rank test, $p = 0.0009$. MM, male to male; MF, male to female; FM, female to male; FF, female to female.