Arch Bronconeumol. 2009;**45(7)**:335-340

ELSEVIER DOYMA

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Original Article

Mortality Analysis of Patients Undergoing Lung Transplantation for Emphysema

Eduardo Miñambres,[a,*] Felipe Zurbano,[b] Sara Naranjo,[c] Javier Llorca,[d] José Manuel Cifrián,[b] and Alejandro González-Castro[a]

[a] *Servicio de Medicina Intensiva, Unidad de Trasplante Pulmonar, Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain*
[b] *Servicio de Neumología, Unidad de Trasplante Pulmonar, Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain*
[c] *Servicio de Cirugía Torácica, Unidad de Trasplante Pulmonar, Hospital Universitario Marqués de Valdecilla, Unidad de Trasplante Pulmonar, Santander, Cantabria, Spain*
[d] *Departamento de Epidemiología y Biología Computacional, Universidad de Cantabria, CIBER Epidemiología y Salud Pública (CIBERESP), Santander, Cantabria, Spain*

ARTICLE INFO

Article history:
Received November 1, 2008
Accepted January 21, 2009
Available online May 20, 2009

Keywords:
Lung transplantation
Emphysema
Prognosis

ABSTRACT

Background: The outcomes of lung transplantation 11 years after starting the transplantation program in our hospital are presented. Risk factors associated with short-, medium-, and long-term mortality in transplant recipients were analyzed.
Patients and Methods: All patients diagnosed with emphysema who underwent lung transplantation between March 1997 and June 2008 were included. The association between different study variables and early death and death at 1 year and 5 years was studied. The Kaplan-Meier method was used to analyze survival. A logistic regression model was used to study the association between early death and variables with a trend towards significance (P<.2) in the univariate analysis. The risk factors for mortality at 1 year and 5 years were analyzed by a Cox regression model.
Results: A total of 92 patients were included. Survival was 89.3%, 70%, and 54% at 1 month, 1 year, and 5 years after transplantation, respectively. Dehiscence of the surgical suture (P<.001), duration of mechanical ventilation in the intensive care unit (P=.04), duration of the surgical procedure (P<.001), and single-lung transplantation (P=.007) were the variables associated with mortality. Extracorporeal circulation and the need for hemodiafiltration in the intensive care unit increased the short-term risk of death (P<.05). The age of the recipient was the variable associated with long-term mortality (P=.02). The duration of the surgical intervention was associated with an increase in short-, medium-, and long-term mortality.
Conclusions: Complications were responsible for short-term mortality, while age of the recipient was the most important factor in determining long-term survival. Mortality was higher in single-lung transplant recipients compared to double-lung transplant recipients.

Trasplante de pulmón en casos de enfisema: análisis de la mortalidad

Palabras clave:
Trasplante pulmonar
Enfisema
Pronóstico

RESUMEN

Introducción: Se presentan los resultados del trasplante pulmonar (TP) en casos de enfisema, tras 11 años desde el inicio del programa de TP, y se analizan los factores de riesgo asociados a la mortalidad a corto, medio y largo plazo en los receptores del trasplante.
Pacientes y métodos: Se ha incluido a todos los pacientes diagnosticados de enfisema que recibieron un TP entre marzo de 1997 y junio de 2008. Se analizó la asociación de las diferentes variables estudiadas con la mortalidad precoz, anual y al quinto año. Se realizó un análisis de supervivencia mediante el método de Kaplan-Meier. Mediante regresión logística se estudió la asociación entre las variables que en el análisis univariante habían mostrado tendencia a la significación estadística (p < 0,2) frente a la mortalidad precoz. Los factores de riesgo para la mortalidad anual y al quinto año se analizaron mediante regresión de Cox.
Resultados: Se incluyó en total a 92 pacientes. La tasa de supervivencia fue del 89,3, el 70 y el 54% al mes, al año y al quinto año del trasplante. La dehiscencia de la sutura quirúrgica (p < 0,001), el tiempo de ventila-

* Corresponding author.
E-mail address: eminambres@yahoo.es (E. Miñambres).

ción mecánica en la Unidad de Cuidados Intensivos (p = 0,04), la duración de la intervención quirúrgica (p < 0,001) y la realización de un trasplante unipulmonar (p = 0,007) fueron las variables asociadas a la mortalidad. El uso de circulación extracorpórea y la necesidad de técnicas de hemodiafiltración en la Unidad de Cuidados Intensivos incrementaron el riesgo de muerte a corto plazo (p < 0,05). La edad del receptor fue la variable asociada a la mortalidad a largo plazo (p = 0,02). La duración de la intervención quirúrgica se asoció a un incremento de la mortalidad a corto, medio y largo plazo.

Conclusiones: Las complicaciones son las responsables del incremento de la mortalidad a corto plazo, mientras que la edad del receptor es la variable que mayor influencia tiene en la mortalidad a largo plazo. Los receptores de un trasplante unipulmonar presentaron un riesgo de fallecimiento mayor que aquellos que recibieron un trasplante bipulmonar.

Introduction

Lung transplantation is indicated in patients with progressive lung disease when pharmacotherapies and other alternatives have failed and when the patient's clinical condition is deteriorating rapidly.[1] However, transplantation is not devoid of major complications in the short, medium, and long term. Emphysema is the main indication for lung transplantation, accounting for 46% of procedures according to the registry of the International Society for Heart and Lung Transplantation (ISHLT).[2] In Spain, chronic obstructive pulmonary disease (COPD) is the main indication for lung transplantation, accounting for 30% of procedures.[3] In developed countries, between 5% and 15% of the population will develop COPD. In Spain, 9% of adults over 40 years of age develop the disease.

Initially, COPD was considered a contraindication for single-lung transplantation for anatomical and physiological reasons. However, in 1988, single-lung transplants were shown to be well tolerated by patients with COPD[4] and the outcomes in terms of morbidity and mortality were satisfactory.[5,6] Today, the decision to perform single-lung transplantation or bilateral lung transplantation in such patients remains a subject of debate in lung transplant groups.[7,8] Although no large differences between these 2 types of lung transplantation have been found, bilateral lung transplantation seems to yield better long-term outcomes,[9,10] especially in patients under 60 years of age.[10]

There is no consensus about the best timing for lung transplantation in a patient with COPD. One-year survival after admission for hypercapnic respiratory failure is no more than 50%, and so such an event would seem an appropriate time to put patients on the waiting list. Most of the centers that perform transplantations have reported that lung transplantation improves survival in patients with COPD,[11-13] although some authors disagree and suggest that survival in transplanted patients is no greater than in untransplanted patients.[14] Recently, the multifactorial BODE index (that is, body mass index, obstruction, dyspnea, and exercise tolerance) has been introduced into clinical practice.[15] This index can help identify the most appropriate moment for a patient with COPD to undergo transplantation.

The objective of this study was to present the results of lung transplantation in patients with COPD in the form of emphysema in our hospital 11 years after the lung transplantation program began. Likewise, the study aimed to analyze the risk factors associated with short-, medium-, and long-term mortality.

Patients and Methods

The study included patients diagnosed with idiopathic emphysema or α-1-antitrypsin-deficiency-related emphysema who underwent lung transplantation in our hospital between March 1997 (when our lung transplantation program began) and June 2008. The management of patients after lung transplantation was based on the protocol established by the lung transplant team in our hospital. Immunosuppressor therapy comprised 3 drugs: cyclosporine or tacrolimus, corticosteroids, and azathioprine (replaced in recent years by mycophenolate). Piperacillin-tazobactam was given as antibiotic prophylaxis. Starting from immediately after the operation, co-trimoxazole was administered for life. Itraconazole or aerosolized amphotericin and ganciclovir were given when the donor or recipient had citomegalovirus infection. This protocol was modified when patients were included in clinical trials.

Follow-up of the recipients included in this study lasted until death or June 15, 2008.

The diagnostic criteria for emphysema were based on the medical history, computed tomography, and lung function testing. Until 2004, the inclusion criteria were forced expiratory volume in 1 second (FEV_1) less than 20% of predicted or frequent admissions for severe pulmonary hypertension and hypercapnia in a basal state (that is, not during an exacerbation). From 2004 onwards, only patients with a BODE score of 7 or more were included. As an exception, patients with a BODE score of less than 7 were included if they had severe pulmonary hypertension, hypercapnia, or repeated admission in the past year. Study data for 92 consecutive transplant recipients were collected. The clinical and laboratory findings, as well as the outcomes for each of these patients, were extracted from the database of the lung transplant team of our hospital.

The variables analyzed were grouped in 4 categories: *a)* demographic and clinical variables of the recipient (age, sex, albumin levels prior to transplantation, emergency lung transplantation, and BODE score); *b)* demographic variables of the donor (age and sex); *c)* variables related to the surgical procedure (duration of surgery, duration of graft ischemia, type of transplant [single-lung or bilateral], use of extracorporeal circulation); and *d)* control variables from the stay in the intensive care unit (ICU), such as PaO_2, fraction of inspired oxygen on admission and after 24 hours in the ICU, use of hemofiltration in the ICU, suture dehiscence in the first few hours, duration of mechanical ventilation in the ICU, and length of stay in the ICU.

Statistical Analysis

A descriptive analysis of the sample was undertaken, with the results presented as numbers and percentages for categoric variables and as means (SD) for continuous ones.

The association between different study variables and early death (first month after surgery) and death at 1 year and 5 years was studied. Means were compared using the *t* test or analysis of variance and proportions were compared with the χ^2 test or the Fisher exact test. A logistic regression model was used to study the association between early death and variables with a trend towards significance ($P<.2$) in the univariate analysis.

Risk factors for 1-year and 5-year mortality were analyzed by stepwise backward Cox regression analysis, including variables with $P<.02$ in the model. The results were expressed as risk ratios (RR) and 95% confidence intervals (CI).

A survival analysis was undertaken considering death as the end point, and a Kaplan-Meier survival curve was plotted for the cohort.

Results

During the study period, a total of 92 lung transplantations were performed for emphysema from a total of 199 procedures. The mean age of the recipients (77 men [83.6%] and 15 women) was 55 years (95% CI, 53-56 years). Twenty patients underwent single-lung transplantation and 72 bilateral lung transplantation. Table 1 shows the main study variables analyzed. Seventy-nine patients (85.9%) had an FEV_1 of 30% or less. The BODE score was at least 7 points in 47% of the patients, 5 or 6 points in 50%, and less than 5 in 3%. Primary graft dysfunction according to ISHLT criteria[16] was detected in 25 patients (27.7%). Of these, 10 (10.8%) had grade 3 (severe) dysfunction, 7 (7.6%) had grade 2 (moderate) dysfunction, and 8 (8.7%) had grade 1 (mild) dysfunction. In all, 19 patients (20.6%) presented bronchiolitis obliterans during their clinical course.

Early mortality (in the first month) in our cohort was 10.7% (95% CI, 3.9%-17.5%; 10 patients). In the univariate analysis of the association between study variables and early mortality, recipients who died early were more likely to have malnutrition and have had longer lung ischemia times as well as a longer duration of surgery. Likewise, the need for extracorporeal circulation during surgery and for hemodiafiltration techniques in the ICU were associated with greater early mortality. Table 2 shows the differences in the analysis of the study variables according to whether patients were alive at 30 days.

Table 1
Characteristics of Study Population[a]

Albumin, g/dL	3.69 (0.70)
Recipient age, y	54.9 (7)
Donor age, y	36.9 (12.3)
Stay in ICU, d	14.8 (23.7)
Hours of the donor on mechanical ventilation	31.6 (45.2)
Duration of ischemia, min	329 (59)
PaO_2/FiO_2 after 24 hours in ICU	322 (100)
Use of extracorporeal circulation	6 (6.5%))
Suture dehiscence	10 (10.8%))
Hemofiltration in ICU	7 (7.6%))
Surgery duration, min	344 (104)
BODE score	6.5 (1.2)
BMI, kg/m^2	23.7 (3.5)
Walk distance, m	261 (98)
Dyspnea grade	3.14 (0.5)
FEV_1 (%)	23 (8)

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in 1 second; FiO_2, fraction of inspired oxygen; ICU, intensive care unit.
[a]Data are shown as means (SD) or numbers of patients (percentages).

In the logistic regression analysis, both the use of hemodiafiltration techniques and extracorporeal circulation increased the risk of death at 1 month among lung transplant recipients. The remaining variables analyzed did not show a significant association with early mortality (Table 2).

Mortality at 1 year was 30% (95% CI, 20.2%-39.9%; 28 patients in total, including those who died in the first month). Table 3 shows the results (univariate analysis) of the variables associated with mortality at 1 year. In the Cox regression analysis, the duration of the surgical intervention, measured in hours, was the only factor associated with mortality at 1 year.

Mortality at 5 years was 46% (95% CI, 35.5%-56.9%; 43 patients in total, including those who had died in the first month and after 1 year). The univariate analysis showed statistically significant differences in the number of hours on mechanical ventilation while in the ICU (P=.01), and the duration of surgery (P=.01) between patients who had died at 5 years after the intervention and those who were still alive (Table 4). The logistic regression model showed that only recipient age and duration of surgery were independently associated with 5-year mortality (Table 4).

The survival curves for the cohort reflect 1-year survival of 69.56% (95% CI, 59.61%-79.51%), 3-year survival of 55.43% (95% CI, 44.73%-66.13%), and 5-year survival of 53.26% (95% CI, 42.52%-64%). The survival curves calculated using the Kaplan-Meier method are shown in the Figure.

The analysis of risk factors using the Cox regression method showed that surgical suture dehiscence in the postoperative period (RR=17.59; 95% CI, 4.64–66.5; P<.001), number of hours on mechanical ventilation while in the ICU (RR=2.09 per unit time; 95% CI, 1.01-4.29; P=.04), duration of the surgical procedure (RR=1.01 per unit time; 95% CI, 1.0067-1.0167; P<.001), and single-lung transplantation vs bilateral lung transplantation (RR=5.88; 95% CI, 1.63-21; P=.007) were the variables most strongly associated with mortality in the cohort. Likewise, the need for renal replacement therapies while in the ICU (RR=6.07; 95% CI, 0.67-54-87; P=.10) and male sex of lung donors (RR=2.69; 95% CI, 0.86-8.39; P=.08) showed a trend towards greater mortality in these patients.

Discussion

Despite improvements in lung graft preservation[17] and postoperative care, the incidence of complications and death in this type of transplantation remains high.[18,19] The ideal time for a patient with COPD to undergo lung transplantation is subject to debate,

Table 2
Mortality at 1 Month[a]

Variable	Alive (n=82)	Dead (n=10)	P	Logistic Regression
Recipient age, y	55.2 (7.2)	52.8 (5.2)	.31	
Female recipient	13 (15.8%)	2 (20%)	.90	
Albumin, g/dL	3.7 (0.6)	3.2 (0.7)	0.04	OR[b]=2.45; 95% CI, 0.75-7.98; P=.13
Emergency transplantation	2 (2.4%)	0 (0%)	–	
Bilateral lung transplantation	62 (75.6%)	10 (100%)	.17	OR=6.89; 95% CI, 0.38-122; P=.17
Donor age, y	37.2 (12.4)	34.9 (11.3)	.57	
Female recipient	22 (26%)	2 (20%)	.93	
Surgery duration, min	344 (90)	473 (132)	<.01	OR=1.32; 95% CI, 0.55-1.82; P=.26
Hours of mechanical ventilation	204 (571)	233 (222)	.87	
Duration of ischemia, min	322 (78)	383 (58)	.01	OR=1.66; 95% CI, 0.30-3.28; P=.38
Use of extracorporeal circulation	3 (3.7%)	3 (30%)	.01	OR=16.55; 95% CI, 1.43-198; P=.02
Use of hemofiltration	4 (4.3%)	3 (30%)	.02	OR=14.11; 95% CI, 1.04-190.65; P=.04
Stay in ICU, d	14.9 (25)	14.4 (9.6)	.94	
PaO_2/FiO_2 at 24 hours	326 (93)	291 (152)	.30	
Suture dehiscence	7 (8.5%)	2 (20%)	.55	
SI for hemorrhage	7 (8.5%)	2 (20%)	.55	

Abbreviations: CI, confidence interval; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; OR, odds ratio; SI, surgical intervention.
[a]Data are shown as means (SD) or number of patients (percentage).
[b]Refers to risk of albumin <3 g/dL vs ≥3 g/dL.

Table 3
Mortality at 1 Year

Variable	Alive (n=64)	Dead (n=28)	*P*	Cox Regression
Recipient age, y	54.5 (7.4)	55.8 (6)	.34	
Female recipient	11 (17%)	4 (14%)	.51	
Albumin, g/dL	3.7 (0.6)	3.5 (0.7)	.36	
Emergency transplantation	2 (3%)	0 (0%)	.87	
Bilateral lung transplantation	50 (77%)	22 (78%)	.92	
Donor age, y	37.4 (12.8)	35.9 (11.2)	.61	
Female donor	19 (29%)	5 (18%)	.37	
Surgery duration, min	334 (79)	414 (130)	<.01	RR=1.43; 95% CI, 1.13-1.82; *P*=.006
Hours of mechanical ventilation	75 (99)	506 (915)	<.01	RR[a]=1.002; 95% CI, 0.99-1.01; *P*=.16
Duration of ischemia, min	331 (77)	324 (82)	.69	
Use of extracorporeal circulation	2 (3%)	4 (14%)	.12	RR=2; 95% CI, 0.48-8.33; *P*=.33
Use of hemofiltration	2 (3%)	5 (18%)	.04	RR=6.1; 95% CI, 0.92-15.66; *P*=.14
Stay in ICU, d	11.8 (20)	21.5 (29.7)	.08	RR[b]=0.96; 95% CI, 0.89-1.04 *P*=.38
PaO_2/FiO_2 24 hours	323 (98)	320 (108)	.89	
Suture dehiscence	2 (3%)	5 (18%)	.01	RR=2.23; 95% CI, 0.73-6.78; *P*=.15
SI for hemorrhage	4 (6.2%)	5 (17.8%)	.17	RR=1.23; 95% CI, 0.40-3.76; *P*=.70

Abbreviations: CI, confidence interval; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; RR, risk ratio; SI, surgical intervention.
[a]Data are shown as means (SD) or number of patients (percentage).
[b]Per unit time.

Table 4
Mortality at 5 Years[a]

Variable	Alive (n=49)	Dead (n=43)	P	Cox Regression
Recipient age, y	53.6 (7.7)	56.3 (5.9)	.18	RR=1.13; 95% CI, 1.01-1.26; *P*=.02
Female recipient	8 (16%)	7 (16%)	.78	
Albumin, g/dL	3.7 (0.7)	3.6 (0.7)	.80	
Emergency transplantation	1 (2%)	1 (2.3%)	.98	
Bilateral lung transplantation	40 (80%)	32 (74%)	.5	
Donor age, y	38.3 (12.6)	35.3 (11.8)	.21	
Female donor	16 (32%)	8 (18%)	.20	RR=0.33; 95% CI, 0.07-1.40; *P*=.13
Surgery duration, min	334 (76)	385 (123)	.01	RR=1.27; 95% CI, 1.06-1.52; *P*=.02
Hours of mechanical ventilation	80 (111)	353 (768)	.01	RR=1.001; 95% CI, 0.99-1.0057; *P*=.11
Duration of ischemia, min	338 (80)	319 (76)	.24	
Use of extracorporeal circulation	1 (2%)	5 (12%)	.15	RR=1.41; 95% CI, 0.38-5.15; *P*=.60
Use of hemofiltration	2 (4.1%)	5 (12%)	.33	
Stay in ICU, d	13.9 (22.5)	15.8 (25.1)	.68	
PaO_2/FiO_2 24 h	333 (95)	310 (106)	.27	
Suture dehiscence	2 (4.1%)	7 (16.3%)	.11	RR=1.33; 95% CI, 0.52-3.41; *P*=.54
SI for hemorrhage	3 (6.1%)	6 (13.9%)	.36	

Abbreviations: CI, confidence interval; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; RR, risk ratio; SI, surgical intervention.
[a]Data are shown as means (SD) or number of patients (percentage).

given that survival cannot be accurately predicted and, in any case, will depend on time on the waiting list and the experience of the hospital staff, among other things.[20,21] Traditionally, the recommendations on when to refer a patient with COPD to the waiting list were the following: FEV_1 after bronchodilation less than 20%, hypercapnia ($PaCO_2$>55 mm Hg), pulmonary hypertension, and individual disease course, with progressive deterioration and/or severe exacerbations.[22] Currently, a BODE score of 7 or more is the most widely used criterion.

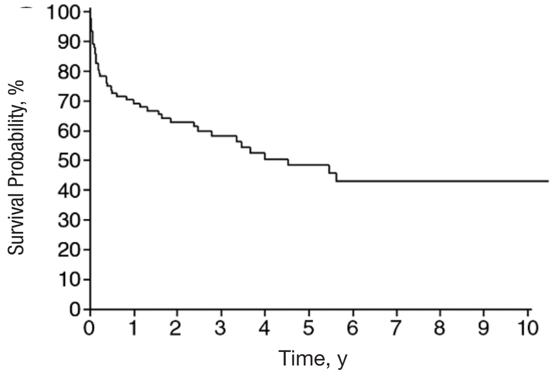

Figure. Crude mortality data: 10 deaths at 1 month, 28 deaths at 1 year, 41 deaths at 3 years, and 43 deaths at 5 years.

Analysis of the survival data in our hospital, in patients undergoing transplantation for emphysema, shows a short-, medium-, and long-term survival comparable to that reported by the ISHLT[10] and by other Spanish transplant groups.[23,24] In addition, the mean age of our recipients is greater than that published by the ISHLT[10] and by other transplant groups in our country.[23-25]

Most recipients, like those of other hospitals in Spain,[26] have a high BODE score (97% ≥5 points). Survival in patients with COPD and a BODE score of 7 or more is 30% at 4 years if they do not undergo lung transplantation.[14,27] Therefore, the survival reported in the present study confirms that patients with COPD and a high BODE score who undergo lung transplantation survive longer than those who do not undergo the procedure.

One of the most interesting aspects of the present study is to compare variables that influence mortality in these patients at different postoperative times (Tables 2-4). Complications (need for extracorporeal circulation and hemofiltration) were the variables associated with increased perioperative mortality, but they did not have an impact on medium- and long-term mortality. The need to resort to extracorporeal circulation during implantation of the lung graft increased the risk of lung injury and increased perioperative mortality.[25,28] Renal failure during the postoperative period was associated with increased postoperative mortality.[29,30]

In the long-term analysis, the variables that influence mortality are different. In the present study, recipient age is one of the variables most strongly associated with increased mortality. This is consistent with the analysis of the ISHLT registry.[2] Although the survival rate in recipients over 60 years of age has been reported to be good, it seems that advanced age of a lung-transplant recipient has been associated with increased mortality, even allowing for age-adjusted life expectancy.[31]

In the present study, a prolonged operation was always associated with increased mortality at all time points, both short term and long term. This association arises essentially because a prolonged time in the operating theater is usually indicative of complications or difficulties. We did not consider analyzing variables that influence mortality beyond 5 years given the limited number of patients in this subgroup (Figure).

One of the most interesting findings of the present study was that patients who received a single-lung transplantation were at greater risk of dying than recipients of a bilateral lung transplantation. This finding should be treated with caution, given that patients who underwent single-lung transplantation were slightly older than those who underwent bilateral lung transplantation, and recipient age influences long-term mortality. Today, the decision to perform single-lung transplantation or bilateral lung transplantation in such patients remains a subject of debate in lung transplant groups.[7,8] Several authors agree that 5-year survival is better in bilateral lung transplantation.[32-33] However, as in our study, the single-lung recipients in those studies were significantly older than the bilateral lung recipients. A recent study by the groups in Toronto, Canada, and Duke University in the United States, showed that bilateral lung transplant recipients had lower rates of bronchiolitis obliterans and a greater long-term survival, even when the patients were stratified by age.[34] Finally, in an analysis of 9883 lung transplant recipients with COPD included in the ISHLT registry, 5-year survival was greater in bilateral lung transplant recipients. This benefit was not apparent in recipients aged 60 years or more.[10] In our series, it was not possible to assess the risk of both types of transplant in these age subgroups given the small number of patients (n=20) who underwent single-lung transplantation. Those in favor of single-lung transplantation in such patients believe that given that surgery is quicker and simpler, with a shorter lung ischemia time, the number of postoperative complications is smaller and mortality in the immediate postoperative period is lower.[35] However, several studies have shown that, although there may be more short-term complications in bilateral lung transplant recipients, the short-term differences in mortality according to the type lung transplantation performed are not significant,[36,37] even in patients aged 60 years or more.[37,38] In contrast, long-term survival seems to be greater in bilateral lung transplant recipients.[10,39]

One of the surprising results of the present study is the trend towards increased mortality with male donors. We do not have an explanation for this finding, though maybe it might be attributable to the limited number of female donors (n=24) and recipients (n=15). A study of the ISHLT registry indicated that different sexes of the donor and recipient could influence prognosis.[40] However, a number of studies have reported opposite results.[41,42] After brain death, numerous endocrine and hormonal changes take place.[43] The theories to support sex matching of the donor and recipient concern the endocrine and hormonal alterations that occur in the donor after brain death, and even the possible protective effect of estrogens (in female donors) in reducing ischemia-reperfusion lesion.[44] Our findings regarding the sex of the donor should be interpreted with caution, and they cannot form the basis of an affirmation that the sex of the donor influences the prognosis of the lung transplant recipient.

In conclusion, our results show that complications in the initial postoperative period were responsible for short-term mortality, while recipient age was the most important factor in determining long-term survival. Patients who received a single-lung transplant were at greater risk of dying than recipients of a bilateral lung transplant, a finding which could have been influenced by the greater age of those receiving single-lung transplant.

References

1. Arcasoy SM, Kotloff RM. Lung transplantation. N Engl J Med. 1999;340:1081-91.
2. Trulock EP, Christie JD, Edwards LB, Boucek MM, Aurora P, Taylor DO, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-fourth official adult lung and heart-lung transplantation report-2007. J Heart Lung Transplant. 2007;26:782-95.
3. Organización Nacional de Trasplantes. Datos de actividad de donación y trasplantes en España. Available from: http://www.ont.es
4. Trulock EP, Egan TM, Kouchoukos NT, Kaiser LR, Pasque MK, Ettinger N, et al. Single lung transplantation for severe chronic obstructive pulmonary disease. Washington University Lung Transplant Group. Chest. 1989;96:738-42.
5. Levine SM, Anzueto A, Peters JI, Cronin T, Sako EY, Jenkinson SG, et al. Medium term functional results of single-lung transplantation for endstage obstructive lung disease. Am J Respir Crit Care Med. 1994;150:398-402.
6. Mal H, Sleiman C, Jebrak G, Messian O, Dubois F, Darne C, et al. Functional results of single-lung transplantation for chronic obstructive lung disease. Am J Respir Crit Care Med. 1994;149:1476-81.
7. Weill D, Keshavjee S. Lung transplantation for emphysema: two lungs or one. J Heart Lung Transplant. 2001;20:739-42.
8. Trulock EP III. Lung transplantation for COPD. Chest. 1998;113 Suppl:269-76.
9. Hadjiliadis D, Angel LF. Controversies in lung transplantation: are two lungs better than one? Semin Respir Crit Care Med. 2006;27:561-6.
10. Thabut G, Christie JD, Ravaud P, Castier Y, Brugière O, Fournier M, et al. Survival after bilateral versus single lung transplantation for patients with chronic obstructive pulmonary disease: a retrospective analysis of registry data. Lancet. 2008;371:744-51.
11. Geertsma A, Ten Vergert EM, Bonsel GJ, De Boer WJ, van der Bij W. Does lung transplantation prolong life? A comparison of survival with and without transplantation. J Heart Lung Transplant. 1998;17:511-6.
12. Charman SC, Sharples LD, McNeil KD, Wallwork J. Assessment of survival benefit after lung transplantation by patient diagnosis. J Heart Lung Transplant. 2002;21:226-32.
13. Thabut G, Ravaud P, Christie JD, Castier Y, Fournier M, Mal H, et al. Determinants of the survival benefit of lung transplantation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2008;177:1156-63.
14. Hosenpud JD, Bennett LE, Keck BM, Edwards EB, Novick RJ. Effect of diagnosis on survival benefit of lung transplantation for end-stage lung disease. Lancet. 1998;351:24-7.
15. Celli BR, Cote CG, Marín JM, Casanova C, Montes de Oca M, Méndez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350:1005-12.
16. Christie JD, Carby M, Bag R, Corris P, Hertz M, Weill D. ISHLT Working Group on Primary Lung Graft Dysfunction. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part II: definition. A consensus statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2005;24:1454-9.
17. Miñambres E, González-Castro A, Rabanal JM, Suberviola B, Ortega FJ, Zurbano F, et al. Comparative study of two preservation solutions in the initial function after bilateral human lung transplantation. Med Intensiva. 2007;31:1-5.
18. González-Castro A, Suberviola B, Llorca J, González-Mansilla C, Ortiz-Melón F, Miñambres E. Prognosis factors in lung transplant recipients readmitted to the intensive care unit. Transplant Proc. 2007;39:2420-1.
19. González-Castro A, Llorca J, Burón J, Suberviola B, Vallejo A, Miñambres E. Evaluation of the oxygenation ratio as long-term prognostic marker after lung transplantation. Transplant Proc. 2007;39:2422-4.
20. Salvatierra Velázquez A. Trasplante pulmonar en España. Arch Bronconeumol. 2004;40 Supl 6:41-8.
21. Borro JM. Actualización del trasplante pulmonar en España. Arch Bronconeumol. 2005;41:457-67.
22. Orens JB, Estenne M, Arcasoy S, Conte JV, Corris P, Egan JJ, et al. International guidelines for the selection of lung transplant candidates. J Heart Lung Transplant. 2006;25:745-55.
23. Algar FJ, Álvarez A, Lama R, Santos F, Baamonde C, Cerezo F, et al. Long-term results of lung transplantation for emphysema. Transplant Proc. 2005;37:1530-3.
24. Cerón-Navarro J, Escrivá-Peiró J, Pastor-Martínez E, Peñalver-Cuesta JC, Ansotegui-Barrera E, Pastor-Colom A, et al. Resultados del trasplante pulmonar en la EPOC tipo enfisema. Arch Bronconeumol. 2008;44:S142-S3.
25. Ferrer J, Rodríguez E, Román A, Bravo C, Roldán J, Hermosilla E, et al. Factors related to postoperative mortality in lung transplantation for emphysema. Transplant Proc. 2007;39:3317-22.

26. Laporta R, Ussetti P, Mora G, López C, Gómez D, de Pablo A, et al. Clinical and functional characteristics of patients prior to lung transplantation: report of experience at the Clínica Puerta de Hierro. Arch Bronconeumol. 2008;44:424-7.
27. Marín JM. Viejos y nuevos criterios para clasificar la EPOC. Arch Bronconeumol. 2004;40 Supl 6:9-15.
28. Cassivi SD, Meyers BF, Bataffarano RJ, Guthrie TJ, Trulock EP, Lynch JP, et al. Thirteen-year experience in lung transplantation for emphysema. Ann Thorac Surg. 2002;74:1663-9.
29. Rocha PN, Rocha AT, Palmer SM, Davis RD, Smith SR. Acute renal failure after lung transplantation: incidence, predictors and impact on perioperative morbidity and mortality. Am J Transplant. 2005;5:1469-76.
30. González Castro A, Llorca J, Suberviola-Cañas B, Fernández-Miret B, Zurbano F, Miñambres E. Acute renal failure in lung transplantation: incidence, correlation with subsequent kidney disease, and prognostic value. Arch Bronconeumol. 2008;44:353-9.
31. Gutiérrez C, Al-Faifi S, Chaparro C, Waddell T, Hadjiliadis D, Singer L, et al. The effect of recipient's age on lung transplant outcome. Am J Transplant. 2007;7:1271-7.
32. Meyer DM, Bennett LE, Novick RJ, Hosenpud JD. Single vs bilateral, sequential lung transplantation for end-stage emphysema: influence of recipient age on survival and secondary end-points. J Heart Lung Transplant. 2001;20:935-41.
33. Günes A, Aboyoun CL, Morton JM, Plit M, Malouf MA, Glanville AR. Lung transplantation for chronic obstructive pulmonary disease at St Vincent's Hospital. Intern Med J. 2006;36:5-11.
34. Hadjiliadis D, Chaparro C, Gutiérrez C, Steele MP, Singer LG, Davis RD, et al. Impact of lung transplant operation on bronchiolitis obliterans syndrome in patients with chronic obstructive pulmonary disease. Am J Transplant. 2006;6:183-9.
35. Low DE, Trulock EP, Kaiser LR, Pasque MK, Dresler C, Ettinger N, et al. Morbidity, mortality, and early results of single versus bilateral lung transplantation for emphysema. J Thorac Cardiovasc Surg. 1992;103:1119-26.
36. Sundaresan RS, Shiraishi Y, Trulock EP, Manley J, Lynch J, Cooper JD, et al. Single or bilateral lung transplantation for emphysema? J Thorac Cardiovasc Surg. 1996;112:1485-94.
37. Miñambres E, Llorca J, Suberviola B, Naranjo S, Zurbano F, González-Castro A. Early outcome following single vs bilateral lung transplant in older recipients. Transplant Proc. 2008;40:3088-9.
38. Nwakanma LU, Simpkins CE, Williams JA, Chang DC, Borja MC, Conte JV, et al. Impact of bilateral versus single lung transplantation on survival in recipients 60 years of age and older: analysis of United Network for Organ Sharing database. J Thorac Cardiovasc Surg. 2007;133:541-7.
39. Chang AC, Chan KM, Lonigro RJ, Lau CL, Lama VN, Flaherty KR, et al. Surgical patient outcomes after the increased use of bilateral lung transplantation. J Thorac Cardiovasc Surg. 2007;133:532-40.
40. Sato M, Gutiérrez C, Kaneda H, Liu M, Waddell TK, Keshavjee S. The effect of gender combinations on outcome in human lung transplantation: the International Society of Heart and Lung Transplantation Registry experience. J Heart Lung Transplant. 2006;25:634-7.
41. Roberts DH, Wain JC, Chang Y, Ginns LC. Donor-recipient gender mismatch in lung transplantation: impact on obliterative bronchiolitis and survival. J Heart Lung Transplant. 2004;23:1252-9.
42. Miñambres E, Llorca J, Subrviola B, Ballesteros MA, Ortiz-Melón F, González-Castro A. Influence of donor-recipient gender mismatch in early outcome after lung transplantation. Transplant Proc. 2008;40:3076-8.
43. Miñambres E, Cemborain A, Sánchez-Velasco P, Gandarillas M, Díaz-Regañón G, Sánchez-González U, et al. Correlation between transcranial interleukin-6 gradient and outcome in patients with acute brain injury. Crit Care Med. 2003;31:933-8.
44. Gabel SA, Walter VR, London RE, Steenbergen C, Korach KS, Murphy E. Estrogen receptor beta mediates gender differences in ischemia/reperfusion injury. J Mol Cell Cardiol. 2005;38:289-97.