ARCHIVOS DE BRONCONEUMOLOGIA

Original Article

Functional Outcomes After Lung Transplant in Chronic Obstructive Pulmonary Disease☆

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ARTICLE INFO

ABSTRACT

Introduction: Lung transplantation (LT) is a therapeutic option with controversial results in chronic obstructive pulmonary disease (COPD). We aimed to analyze the outcomes of transplantation in terms of lung function and to identify prognostic factors.

Method: A retrospective analysis of 107 patients with COPD receiving lung transplants in the La Fe Hospital between 1991 and 2008 was performed. Preoperative variables, functional examinations pre and post-LT, surgical procedure variables and long-term monitoring, expressed as mean or percentage, as applicable, were analyzed. Spirometric results before and after LT were analyzed. Linear or logistic regression was used for multivariate analysis depending on the variable.

Results: Ninety-four men (87.9%) and 13 women (12.1%) were transplanted, with a mean age±standard deviation of 52.58±8.05 years; 71% of LTs were double-lung transplantations. Spirometric values improved after LT: FVC: +1.22 L (+34.9%), FEV_1: +1.66 L (+56.7%) and FEF_{25-75}: +1.85 L (+50.8%); P=.001. This functional improvement was maintained after 5 years only in the group with BODE score >7 (P=.001). Recipient height, type of LT, use of extracorporeal circulation during the surgical procedure, presence of bronchiolitis obliterans syndrome and the age and cause of death of the donor significantly influenced lung function over time.

Conclusions: LT improves lung function in COPD patients. This improvement was maintained at 5 years only in patients with BODE>7. Double lung transplantation provides better functional results than single-lung transplantation.

Resultados funcionales del trasplante pulmonar en la enfermedad pulmonar obstructiva crónica

RESUMEN

Introducción: El trasplante pulmonar (TP) es una opción terapéutica con resultados controvertidos en la enfermedad pulmonar obstructiva crónica (EPOC). Nuestro objetivo es analizar los resultados del trasplante en términos de función pulmonar, así como identificar los factores pronósticos.

Método: Se realizó un análisis retrospectivo de 107 pacientes con EPOC trasplantados en el Hospital Universitario La Fe entre 1991 y 2008. Se analizaron variables preoperatorias, estudio funcional pre y post-TP, variables del procedimiento quirúrgico y del seguimiento a largo plazo, expresadas en media o porcentaje según el caso, comparándose los resultados espirométricos antes y después del TP. Para el análisis multivariante se utilizó regresión lineal o logística según la variable.

Resultados: Fueron trasplantados 94 hombres (87,9%) y 13 mujeres (12,1%), con una edad media±desviación estándar de 52,58 ± 8,05 años; el 71% de TP fueron bipulmonares. Los valores espirométricos mejoraron tras el TP: FVC: +1,22 l (+34,9%), FEV₁: +1,66 l (+56,7%) y FEF₂₅₋₇₅: +1,85 l (+50,8%); p = 0,001, manteniéndose esta mejoría funcional tras 5 años solo en el grupo con puntuación BODE > 7 (p = 0,001). La talla del receptor, el tipo de TP, la utilización de circulación extracorpórea durante el procedimiento quirúrgico, la presencia de síndrome de bronquiolitis obliterante junto con la edad y la causa de muerte del donante influyeron significativamente en la función pulmonar a largo plazo.
Conclusiones: El TP mejora la función pulmonar de los pacientes con EPOC. Esta mejoría se mantiene a los 5 años solo en los pacientes con BODE mayor de 7. El trasplante bipulmonar proporciona mejores resultados funcionales que el unipulmonar.

Introduction

Chronic obstructive pulmonary disease (COPD) is a health problem of the first magnitude, and is currently estimated to be the fourth cause of death worldwide. Incidence of COPD is on the rise, and in the near future it will take third place in the global mortality ranking.[1,2]

Despite constant advances and updates in the treatment of this disease,[1,3–5] COPD is one of the few chronic diseases that has shown an increase in mortality in recent years.[6]

In the last few decades, lung transplantation (LT) has been a therapeutic alternative in patients with end-stage disease and with chronic respiratory failure,[5,7] and this procedure has yielded 5-year survival rates of around 50% in highly selected patients.[7,8]

However, the use of this intervention in COPD remains controversial. Several authors have reported the efficacy of LT in terminal disease, both in terms of survival and quality of life,[8–11] while other have questioned the usefulness of the procedure in this entity,[4,12] since it yields the poorest outcomes in terms of long-term survival, matched only by pulmonary fibrosis.[7,13]

The latest report of the International Society for Heart and Lung Transplantation (ISHLT) (2013)[7] analyzes the functional status of patients receiving LT according to the Karnofsky scale, and their reincorporation into the workplace. However, very few studies have analyzed the course of lung function in recipients, determined by spirometry, over the years following LT.[8]

The aim of this study was to analyze the evolution of lung function values in COPD patients undergoing LT, and to identify variables that may affect their outcome.

Method

This was a retrospective analysis of 107 COPD patients undergoing lung transplantation in the Hospital Universitario La Fe, from the introduction of the transplantation program in 1991 up to December 31, 2008. Follow-up comprised the period between the performance of the procedure and the death of the patient, or for survivors, until the date of study closure on January 1, 2010.

The clinical diagnosis of COPD was made on the basis of current international guidelines[3] or those in force at the time of diagnosis. All patients accepted for LT were included in the program on the basis of established international criteria.[14]

The following pre-operative variables were analyzed: age, sex, height, weight, body mass index (BMI), accumulated tobacco use expressed in pack-years, diagnosis (COPD or alpha-1-antitripsin deficit [A1ATD]), BODE index,[15] full evaluation of respiratory function, including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁) forced expiratory flows (FEF₂₅₋₇₅), residual volume to total lung capacity ratio (RV/TLC), suggestive of pulmonary hypersufflation, and carbon monoxide diffusing capacity (DLCO), all of which were expressed in liters and percentage, and 6-min walking test in meters. Donor age and cause of death were recorded,

Table 1
Demographic Characteristics of Recipients and Donors.

Recipient		Donor	
Age, years	52.58±8.05	*Age, years*	35.06±13.89
Sex ♂/♀, %	87.9/12.1	*Sex ♂/♀, %*	82.2/17.8
Type of LT		*Cause of death (%)*	
Single-lung, n (%)	31 (29)	TBI	48.6
Double-lung, n (%)	76 (71)	CVA	45.8
BODE, n (%)		Other	5.6
>7	81 (75.7)	PaO₂/FiO₂	471±80.5
<7	26 (24.3)		
Time of ischemia (min)	294±57.1		
Use of ECC, n (%)	15 (14)		

CVA: cerebrovascular accident; ECC: extracorporeal circulation; PaO₂/FiO₂: partial pressure of oxygen in arterial blood/fraction of inspired oxygen ratio; LT: lung transplantation; TBI: traumatic brain injury.

together with intra-operative variables such as type of intervention, single-lung transplantation (SLT) or double-lung transplantation (DLT) and use of extracorporeal circulation (ECC).

The following variables were collected in each of the scheduled visits during the immediate perioperative phase and in the protocolized follow-up, 1, 3 and 6 months, and 1, 2 and 5 years post-LT, or until death: partial pressure of oxygen in arterial blood/fraction of inspired oxygen ratio (PaO₂/FiO₂), 6 and 48 h after LT, BMI, and signs of bronchiolitis obliterans syndrome (BOS)[16] suggestive of chronic graft rejection, and the above-mentioned lung function values.

Analysis and comparison of means for continuous quantitative variables were performed using the Student's *t*-test[17] for independent or paired samples for related means. Analysis of variance (ANOVA) was used to compare the quantitative variables of several groups.

The chi-squared[17] method was used for analysis and comparison of qualitative variables, or, if conditions for chi-squared validity were not met, Fisher's exact test was used.

The multivariate analysis was performed using the linear regression test for continuous quantitative variables and the logistics regression test for qualitative variables.

Statistical significance was set at $P \leq .05$.

Results

A total of 94 men (87.9%) and 13 women (12.1%) with a mean age±standard deviation of 52.58±8.05 were transplanted. A total of 92 patients (86%) of patients had COPD, while 15 patients (14%) had a diagnosis of A1ATD. The most important characteristics of recipients and donors are described in Table 1.

The mean height of recipients was 1.66±0.72 m, weight was 63.57±11.46 kg, and BMI 22.84±3.22 kg/m².

Results of lung function tests and pre-LT blood gases are given in Table 2.

Of the transplantations, 76 (71%) were double-lung. ECC was necessary in 14% of procedures, all of which were DLT. Mean donor