Clinical and Functional Characteristics of Patients Prior to Lung Transplantation: Report of Experience at the Clínica Puerta de Hierro

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OBJECTIVE: The time at which lung transplantation is indicated is determined by clinical and functional criteria that vary according to the particular disease. The aim of our study was to present the criteria according to which patients were placed on waiting lists for lung transplantation in our hospital.

PATIENTS AND METHODS: We analyzed retrospectively the clinical characteristics, lung function, heart function, and 6-minute walk test results of patients who had received a lung transplant in our hospital from January 2002 through September 2005.

RESULTS: During the study period 100 lung transplants were performed. The mean age of the patients was 45 years (range, 15-67 years) and 57% were men. The diseases that most often led to a lung transplant were chronic obstructive pulmonary disease (COPD) (35%), pulmonary fibrosis (29%), and bronchiectasis (21%). Lung function values differed by disease: mean (SD) forced expiratory volume in 1 second (FEV_1) was 20% (11%) and forced vital capacity (FVC) was 37% (15%) in patients with COPD; FEV_1 was 41% (15%) and FVC, 40% (17%) in patients with pulmonary fibrosis; and FEV_1 was 23% (7%) and FVC, 37% (10%) in patients with bronchiectasis.

CONCLUSIONS: The patients who received lung transplants in our hospital were in advanced phases of their disease and met the inclusion criteria accepted by the various medical associations when they were placed on the waiting list.

Key words: *Lung transplantation. Lung disease. Spirometry. Selection of patients.*

Características clínicas y funcionales antes del trasplante pulmonar. Experiencia en la Clínica Puerta de Hierro

OBJETIVO: El momento para indicar un trasplante pulmonar está definido por criterios clínicos y funcionales diferentes para cada enfermedad. El objetivo de este estudio es presentar cuáles fueron los criterios por los que en nuestro hospital se incluyó a los pacientes en lista de espera de trasplante pulmonar.

PACIENTES Y MÉTODOS: Se ha realizado un análisis retrospectivo de las características clínicas, la función respiratoria, la prueba de la marcha de 6 minutos y el estudio cardiológico de los pacientes que recibieron un trasplante pulmonar entre enero de 2002 y septiembre de 2005.

RESULTADOS: En el período estudiado se realizaron 100 trasplantes pulmonares. La edad media de los pacientes era de 45 años (rango: 15-67) y el 57% eran varones. Las enfermedades que con mayor frecuencia motivaron el trasplante pulmonar fueron la enfermedad pulmonar obstructiva crónica (EPOC, 35%), la fibrosis pulmonar (29%) y las bronquiectasias (BQ) (21%). La media ± desviación estándar de la función pulmonar osciló entre el 20 ± 11% del volumen espiratorio forzado en el primer segundo (FEV_1) y el 37 ± 15% de la capacidad vital forzada (FVC) en la EPOC; del 41 ± 15% del FEV_1 y el 40 ± 17% de la FVC en la fibrosis pulmonar, y del 23 ± 7% del FEV_1 y el 37 ± 10% de la FVC en las BQ.

CONCLUSIONES: Los pacientes que recibieron un trasplante pulmonar en nuestro centro se encontraban en fases muy evolucionadas de su enfermedad y cumplían los criterios de inclusión admitidos por las diferentes sociedades médicas cuando se les incluyó en lista de espera.

Palabras clave: *Trasplante pulmonar. Enfermedad pulmonar. Espirometría. Selección de pacientes.*

Introduction

In patients with advanced lung disease, lung transplantation is a therapeutic option when other treatments fail. The timing or window of opportunity for transplantation is considered to have been reached when the patient is expected to survive longer with a transplant than without one. It is difficult to determine the right time for lung transplantation in each specific patient, given that estimation of survival cannot be measured exactly and that other factors, such as length of time on the waiting list and the experience of the hospital, may influence the decision.[1,2] The various medical associations dedicated to lung transplantation have recently revised their recommendations regarding the timing of

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transplantation in various diseases, according to clinical and functional criteria.[3,4]

The aim of our study was to present the clinical and functional characteristics according to which patients were accepted for lung transplantation at the Hospital Universitario Clínica Puerta de Hierro, Madrid, Spain from January 2002 through September 2005.

Patients and Methods

We retrospectively studied all patients who received a lung transplant between January 2002 and September 2005 in the Hospital Universitario Clínica Puerta de Hierro. A medical history, using a standard data collection sheet, was taken of all patients. The test complement included lung function tests (spirometry, plethysmography, and measurement of carbon monoxide diffusing capacity), baseline arterial blood gas analysis, 6-minute walk test, and heart function tests (electrocardiogram, echocardiogram, and cardiac catheterization with coronary arteriography in patients with cardiovascular risk factors).

Functional class was determined according to the New York Heart Association[5] scale and the patient's physical activity was assessed according to the physician's subjective evaluation of the presence and intensity of dyspnea during the interview. The degree of dyspnea was assessed using the Medical Research Council[6] dyspnea scale, a questionnaire designed to measure symptom severity.

The variables analyzed because of their influence on the selection of lung transplant recipients were forced expiratory volume in 1 second (FEV_1), forced vital capacity, total lung capacity, residual volume, PaO_2, $PaCO_2$, pulmonary artery systolic pressure estimated by echocardiography, and number of meters walked in the 6-minute walk test. In patients with chronic obstructive pulmonary disease (COPD) we used the BODE index,[7] which integrates body mass index (BMI), airflow obstruction, dyspnea, and exercise capacity. The index can predict risk of death according to the scores obtained in these parameters.

Statistical Analysis

The SSPS statistical program was used to process data. Quantitative variables were compared using the *t* test and qualitative variables using the χ^2 test or Fisher exact test when necessary. Statistical significance was set at a value of *P* less than .05.

Results

During the study period 100 lung transplants were performed. The diseases that most frequently led to lung transplantation (Figure 1) were COPD (35%), pulmonary fibrosis (29%), and bronchiectasis (21%). Lung transplant was bilateral in 67% of cases and unilateral in 33% (Figure 1). The mean age of the patients was 45 years (range, 15-67 years) and 57% were men. The mean BMI was 24 kg/m^2 (range, 16-31). Grouped according to disease, the mean (SD) BMI was higher in patients with pulmonary fibrosis (27 [5] kg/m^2) compared to other diseases (Table).

At the time they were placed on a waiting list, 54% of patients were in functional class III, 43% in class IV, and the remaining 3% in class II. The 3 patients in class II had cystic fibrosis. Two of them had repeated pneumothorax and the third presented life-threatening hemoptysis despite having undergone embolization.

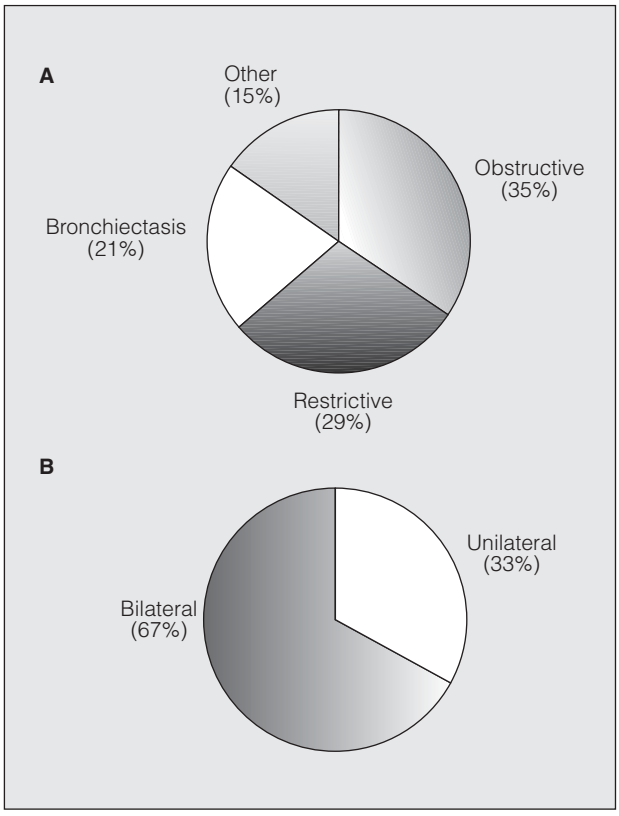

Figure 1. Distribution, in percentage, of diseases that most often led to lung transplant (A) and percent distribution of transplant type, (unilateral or bilateral) (B).

Associated cardiovascular risk factors were analyzed. Hypercholesterolemia was found in 18% of patients, arterial hypertension in 16%, and diabetes mellitus in 6%. Fifteen percent of patients had a combination of 2 of these risk factors and 14% a combination of 3 of them. In our program, when 2 or more cardiovascular risk factors (arterial hypertension, hypercholesterolemia, diabetes mellitus, and age more than 55 years) are present in combination, coronary arteriography is indicated in order to detect lesions that might need to be repaired prior to transplantation. Fifteen patients underwent coronary arteriography and we detected coronary obstruction requiring stent placement in 2 of them. In no case was a lung transplant contraindicated.

A right heart study is not part of the routine protocol for pretransplant evaluation in our unit. Nevertheless, it was performed in those patients requiring coronary arteriography (n=15). The pulmonary artery systolic pressure obtained in the right heart study was comparable to that obtained by echocardiography.

The Table shows mean lung function values according to disease. Of note were the FEV_1 values, which were around 20% of predicted in patients with COPD or bronchiectasis. Mean values for the 6-minute walk test are also shown in the Table. It can be observed that patients with bronchiectasis, despite their much deteriorated lung function, walked a longer distance.

TABLE
Clinical and Functional Characteristics of Lung Transplant Recipients[a]

	Age, y	BMI, kg/m²	FVC		FEV_1		6 Minute Walk Test, m	PaO_2 mm Hg	$PaCO_2$ mm Hg		PASP < 30 mm Hg
			mL	% of Predicted	mL	% of Predicted			mL	% of Predicted	
COPD	50 (12)	24 (7)[b]	1731 (840)	37 (15)	699 (418)	20 (11)	54	264 (89)	49 (5)	48 (11)	47
Pulmonary fibrosis	53 (7)	27 (5)[b]	1606 (765)	40 (17)	1310 (541)	41 (15)[b]	102	298 (90)	46 (9)	41 (6)	41
Bronchiectasis	29 (13)[b]	20 (3)[b]	1637 (502)	37 (10)	848 (266)	23 (7)	62	335 (133)	53 (6)	44 (7)	14
Total	45 (14)	24 (3)	1694 (67)	38 (14)	962 (524)	28 (11)	73	289 (105)	49 (7)	44 (9)	–

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PASP, pulmonary artery systolic pressure estimated by echocardiography.
[a]Data are expressed as means (SD).
[b]$P<.05$.

Pulmonary hypertension (pulmonary artery systolic pressure >30 mm Hg) was found in 47% of patients with COPD and in 41% of those with pulmonary fibrosis (Table). The high prevalence of pulmonary hypertension in this series was due to the fact that it is one of the criteria for performing lung transplantation in these diseases. Finally, 74% of patients with COPD were found to have a BODE index of 7 or higher (Figure 2).

Discussion

Our results showed that patients who received transplants in our unit were in very advanced phases of their disease, both functionally and clinically, at the time they were placed on a waiting list.

Medical associations devoted to lung transplantation have published recommendations for the selection of candidates according to groups of diseases.[3] Patients with COPD are recommended to be placed on a waiting list when the following criteria are met: postbronchodilator FEV_1 less than 20%, hypercapnia ($PaCO_2$ >55 mm Hg), pulmonary hypertension, and progressive deterioration or severe exacerbations.[8] The survival benefit derived from following these recommendations in patients with COPD has been called into question, and consequently other alternatives for indicating transplantation in such patients need to be explored.[9] The multifactorial BODE index, created by Celli et al,[7] can predict survival in COPD patients. The 4-year survival rate of COPD patients with a BODE score of 7 or higher is only 30%. Since the 4-year survival rate after lung transplantation is more than 50%,[10] patients with a BODE score of 7 or higher can benefit from a transplant. In our hospital we have incorporated the BODE score into our decision-making process regarding the time lung transplant should be performed in patients with this disease. We observed that 74% of patients had a BODE score of 7 or higher when they were placed on waiting lists.

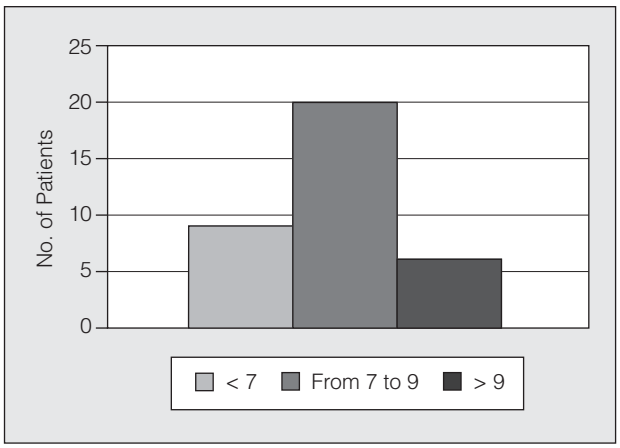

Figure 2. Distribution of BODE scores in lung transplant recipients with chronic obstructive pulmonary disease.

In patients with restrictive lung disease, it is difficult to establish an ideal time at which transplantation is indicated,[1,12] although there are functional criteria that can help predict prognosis.[13,14] However, due to the rapid deterioration that characterizes restrictive lung disease and the high mortality rate in patients on a waiting list,[9,15] the decision to perform a transplant is taken with patients in a functional class indicative of an earlier disease stage. Thus, some authors recommend referring patients with usual interstitial pneumonia to a transplant unit at the time of diagnosis.[16]

In suppurative lung diseases, especially cystic fibrosis, referral for lung transplantation is recommended when FEV_1 is less than 30%,[17,18] or when there is hypercapnia, marked hypoxemia, or a rapid decrease in FEV_1.[19] Other factors to be taken into consideration are frequency of exacerbations,[20] progressively poor nutrition, and female sex.[21-23]

In conclusion, patients who received lung transplants in the Hospital Universitario Clínica Puerta de Hierro met the clinical and functional criteria accepted by the various medical associations when they were placed on the waiting list. In view of the survival results for each of the diseases, we tend to delay referral for a lung transplant in obstructive lung diseases and refer patients earlier on in suppurative and restrictive lung diseases.

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