



Original Article

Characteristics of Candidates for Lung Transplantation Due to Chronic Obstructive Pulmonary Disease and Alpha-1 Antitrypsin Deficiency Emphysema[☆]



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ARTICLE INFO

Article history:

Received 20 June 2014

Accepted 5 August 2014

Available online 6 June 2015

Keywords:

COPD

Alpha-1 antitrypsin deficiency

Lung transplantation

ABSTRACT

Introduction: COPD and emphysema due to alpha-1 antitrypsin deficiency (AATD) are the first and fourth indications for lung transplantation worldwide, respectively. Despite this, there is little information regarding the health status of these patients at the time of transplantation.

Methods: Patients who received a lung transplant in the Hospital Vall d'Hebron between July 1993 and August 2013 were identified and data from the evaluation prior to the transplant were collected.

Results: A total of 217 patients who received a lung transplant for COPD and 19 in whom the indication was AATD were included. These patients were severely impaired at the time of the evaluation for lung transplantation, although the trend in recent years has been to evaluate patients at earlier stages of the disease.

Baseline characteristics were similar in both groups except that patients with AATD were younger [43 (7.7) vs 53.6 (6.1) years old, $P < .001$], with less exposure to tobacco [23.9 (15) vs 50 (29) packs-year, $P < .002$] and lower PCO_2 [41.7 (7.6) vs 47.9 (9.7) mmHg, $P < .004$].

Conclusions: The number of patients receiving a lung transplant for COPD has progressively increased and the tendency is to perform the evaluation in earlier stages of the disease. Patients receiving transplants for COPD and AATD had similar characteristics at the time of the evaluation, although AATD patients were younger and had less exposure to tobacco and lower PCO_2 .

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Características de la población candidata a trasplante pulmonar por enfermedad pulmonar obstructiva crónica y por enfisema secundario a déficit de alfa 1 antitripsina

RESUMEN

Introducción: La EPOC y el enfisema secundario a déficit de alfa-1 antitripsina (DAAT) son la primera y la cuarta causa de trasplante pulmonar en el mundo, respectivamente, a pesar de lo cual disponemos de poca información sobre la situación en la que estos pacientes llegan al trasplante.

Métodos: Se identificó a los pacientes trasplantados por EPOC y por enfisema secundario a DAAT en el Hospital Vall d'Hebron entre julio de 1993 y agosto de 2013 y se recogieron datos de la evaluación previa al trasplante.

Resultados: Se incluyó a un total de 217 pacientes trasplantados por EPOC y 19 por enfisema secundario a DAAT. Los pacientes evaluados para trasplante por estas enfermedades presentaban una afectación

Palabras clave:

EPOC

Déficit de alfa-1 antitripsina

Trasplante pulmonar

[☆] Please cite this article as: Giacoboni D, Barrecheguren M, Esquinas C, Rodríguez E, Berastegui C, López-Meseguer M, et al. Características de la población candidata a trasplante pulmonar por enfermedad pulmonar obstructiva crónica y por enfisema secundario a déficit de alfa 1 antitripsina. Arch Bronconeumol. 2015;51:379–383.

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grave de su enfermedad aunque en los últimos años se observó una tendencia a realizar la evaluación en estadios más precoces. Ambos grupos presentaban características similares, excepto que los pacientes con DAAT eran más jóvenes (43 [7,7] vs. 53,6 [6,1] años; $p < 0,001$), con un menor consumo de tabaco (23,9 [15] vs. 50 [29] paquetes/año; $p = 0,002$) y menor PCO_2 (41,7 [7,6] vs. 47,9 [9,7] mmHg, $p = 0,004$).
Conclusiones: El número de pacientes trasplantados por EPOC ha aumentado progresivamente, observándose una tendencia a realizar la evaluación de trasplante en estadios más tempranos de la enfermedad. Los pacientes evaluados para trasplante por EPOC y por enfisema secundario a DAAT presentan características similares, aunque estos últimos eran más jóvenes, tenían un menor consumo de tabaco y menor PCO_2 .

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Introduction

A total of 37 581 lung transplants were carried out worldwide between January 1995 and June 2012, 12 602 (33.5%) of which were due to chronic obstructive pulmonary disease (COPD), the most common reason for lung transplant, followed by idiopathic pulmonary fibrosis and cystic fibrosis. The COPD group does not include patients undergoing transplant for emphysema secondary to alpha-1 antitrypsin deficiency (AATD), which itself is the fourth indication for lung transplant, with 2182 transplants conducted during this period, accounting for 5.8% of the total.¹

AATD is a genetic disease that is associated with low levels of alpha-1 antitrypsin (AAT) in blood and tissues, and predisposes the individual to lung and liver disease.² AATD emphysema is the most common potentially fatal congenital disease in adulthood, and is also the most common cause of morbidity and mortality in patients with severe AATD. Up to one third of patients have significant disability at a young age due to the respiratory disease, and survival of these patients is lower than that of the general population.³ It is usually detected in advanced stages of the disease, so it is highly underdiagnosed.⁴

Medical treatment of patients with AATD emphysema should include pharmacological and non-pharmacological measures common to COPD patients. Moreover, purified AAT from donor plasma for intravenous administration has been available since 1987. The aim is to raise AAT levels in plasma and lung interstitium to prevent destruction of the parenchyma, and arrest the progression of emphysema in selected patients.²

Patients with COPD with or without AATD who present with significant functional deterioration may benefit from lung transplantation, primarily to improve survival, although there is little information on transplantation for AATD.⁵ The aim of this study was to describe the characteristics of patients with AATD emphysema on their arrival for lung transplantation compared to those of patients who received a transplant for COPD. We also describe any changes observed in the clinical characteristics of patients evaluated for transplantation from the start of the lung transplant program to the present day.

Methods

A cross-sectional observational study was conducted in patients evaluated for lung transplantation for COPD with and without AATD in Hospital Universitari Vall d'Hebron (Barcelona, Spain) between July 1993 and August 2013.

The study was carried out according to the principles of the Declaration of Helsinki and current regulations for conducting research studies in human subjects. Patient confidentiality was maintained at all times, in compliance with Spanish law 15/1999 on Data Protection.

The following data were collected at the time of the transplant evaluation: medical history, sociodemographic and clinical data,

and the findings of lung function tests, arterial blood gases and 6-minute walk test (6-MWT).

Lung function tests were carried out using the MasterLab system (MasterLab, Jaegger, Germany), following the recommendations of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).⁶ The 6-MWT, standardized according to international recommendations, was used to evaluate exercise capacity.⁷

Statistical Analysis

Before analysis, quality control was carried out to identify anomalous data in each variable. Frequency and valid percent were determined in the case of the qualitative variables. Central tendency (mean, median), position (quartiles) and dispersion measures (standard deviation and interquartile range [IQR]) were calculated for the quantitative variables.

In the case of qualitative variables, patient characteristics were compared according to the year of transplant or group (COPD with or without AATD) using the Chi-squared test or Fisher's test (if the observed frequency was < 5). In the case of ordinal variables, the linear trend was determined using Kendall's Tau-c coefficient. Quantitative variables were compared using the Student's *t*-test (< 2 categories) and analysis of variance (ANOVA) (in the case of variables > 2 categories), linear trend test and multiple comparisons test (Scheffé). Analysis was performed using the SPSS 19.0 statistics package (Chicago, IL, USA). A significant difference was determined for all tests based on a *P* value $< .05$.

Results

A total of 695 lung transplants were performed in Hospital Vall d'Hebron from 1993 to 2013. Of these, 31.2% ($n = 217$) were carried out in patients with COPD and 8% ($n = 19$) in patients with AATD emphysema. Patients with AATD had homozygous PiZZ phenotype in 18 cases, and 1 was homozygous for the rare PiY_{Barcelona}⁸ variant.

Patients included in the study had a mean age of 53.1 (SD: 6.6) years at the time of the lung transplant evaluation, and 80% ($n = 189$) were men. As regard smoking, 95.3% of patients were former smokers and 2.1% were current smokers; mean cumulative tobacco exposure was 48 pack-years (SD: 29). Mean FEV_1 (%) was 22.3% (SD: 8.8%). Arterial blood gases showed PO_2 60 mmHg (SD: 10.8) and $PaCO_2$ 47.4 mmHg (SD: 9.7). The mean distance walked in the 6-MWT was 231.4 m (SD: 86.6). A total of 87.2% of patients were on long-term home oxygen therapy.

A trend toward an annual increase in the number of lung transplants for COPD was observed, with a higher frequency in 2008, 2010 and 2012 (Fig. 1).

To measure trends over time in patients referred for lung transplantation, the study was divided into 3 periods. Patients evaluated for transplantation in the last period (2009–2013) were older ($P = .001$), with a lower percentage of men ($P = .001$), with less FEV_1 decline (*L* and %) ($P = .038$ and $P < .001$, respectively), better

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