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Original article

Perioperative mortality of lung transplantation in chronic obstructive pulmonary disease☆

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ABSTRACT

Introduction: Lung transplantation (LT) has been considered an alternative therapeutic approach in terminal patients. However, this process in COPD is not controversy-free. This paper aimed to analyse 30-day mortality (PM) patterns and their risk factors in COPD patients undergoing LT.
Patients and method: A retrospective cohort with 107 COPD patients, transplanted at the University La Fe Valencia, Spain, treated from January 1991 to December 2008. Demographics values, degree of dyspnoea, diagnosis, BODE index, single versus bilateral LT, cardio-pulmonary bypass, donor age, steroid dependence, presence of bronchiectasis, retrograde perfusion, transfusion of blood products, and PaO_2/FiO_2 were analysed. Continuous variables were expressed as mean ± SD and categorical variables as absolute frequency and percentage. A Cox regression model was used for multivariate analysis.
Results: Ninety-four men and 13 women of a mean age of 52.58 ± 8.05 years were transplanted. Of all patients, 75% obtained a BODE score above 7. There were 76 bilateral LT. PM was established at 14%. Main causes of death were infection (53.3%) and surgical complications (33.3%). Presence of bronchiectasis and chronic use of corticosteroids, donor/recipient difference in size and presence of fat in retrograde perfusion fluid were important risk factors for PM. Moreover, PaO_2/FiO_2 ratio at 6 h was a protective factor for the event, thus a higher ratio value, lowered the risk of PM.
Conclusions: LT is a procedure with a high PM rate. Use of corticosteroids, the presence of bronchiectasis and fat emboli in the retrograde reperfusion, and PaO_2/FiO_2 significantly determine PM.

Mortalidad perioperatoria del trasplante pulmonar en la enfermedad pulmonar obstructiva crónica

Palabras clave:
Enfermedad pulmonar obstructiva crónica
Trasplante pulmonar
Mortalidad perioperatoria

RESUMEN

Introducción: El trasplante pulmonar (TP) es una alternativa terapéutica en pacientes con EPOC en fase terminal. Nuestro objetivo es analizar la mortalidad perioperatoria (30 días) (MP) y los factores de riesgo que la condicionan en pacientes con EPOC sometidos a TP.
Pacientes y método: Cohorte retrospectiva de 107 pacientes con EPOC trasplantados en el Hospital Universitario La Fe (1991-2008). Los datos demográficos, el grado de disnea, el diagnóstico, el índice BODE, el tipo de trasplante, la circulación extracorpórea, la edad del donante, la dependencia de glucocorticoides, la presencia de bronquiectasias, la reperfusión retrógrada, la transfusión de hemoderivados y la relación PaO_2/FiO_2 fueron analizadas. Las variables continuas se expresaron como media ± DE y las categóricas, con frecuencias absolutas y porcentajes. El análisis multivariante se realizó mediante el modelo de regresión de Cox.

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Resultados: Se trasplantaron 94 hombres y 13 mujeres con una edad media de 52,58 ± 8,05 años. El 75% de los pacientes tuvieron un BODE ≥ 7. Se realizaron 76 procedimientos bipulmonares. La MP fue del 14%. Las causas de muerte fueron las infecciones (53,3%) y las complicaciones quirúrgicas (33,3%). La presencia de bronquiectasias, el uso de glucocorticoides, la diferencia de talla entre receptor/donante y la presencia de émbolos grasos en la reperfusión retrógrada fueron factores de riesgo para la MP. La relación de PaO_2/FiO_2 a las 6 h fue un factor protector para la MP.
Conclusiones: El TP es un procedimiento con una elevada tasa de MP. El uso previo de glucocorticoides, la presencia de bronquiectasias y de émbolos grasos en la reperfusión retrógrada, así como la PaO_2/FiO_2 condicionaron la MP.

Introduction

Chronic obstructive pulmonary disease (COPD) is a serious health problem that is currently considered to be the fourth leading cause of death worldwide. Given its increasing incidence, it is expected to rank third in the causes of global death over the coming years.[1] In addition to its high prevalence, the disease also has an impact because of high associated morbidity and mortality[2,3] and its significant socioeconomic impact.

Lung transplantation (LT) has recently been considered a therapeutic alternative for patients in terminal stages of the disease who have chronic respiratory failure, with survival rates at around 50% at 5 years of LT.[4,5] However, this procedure is not without controversy. Several authors have reported the efficacy of LT in the final stages of the disease, both in terms of survival and quality of life,[4,6,7] while others have questioned the usefulness of this procedure in COPD[8] because, in addition to pulmonary fibrosis, it has the worst results in terms of survival.[5]

LT is a surgical procedure with high perioperative mortality (PM) (30-day mortality). Most authors report a PM rate of between 5 and 18%,[6] although this extreme is not systematically reflected in the majority of published papers related to LT. Early mortality is a difficult parameter to specify in the medical literature, as there are multiple ways to express it – mortality within the first 24 h, mortality within the first 60 or 90 days[5] – which make it difficult to compare results homogeneously.

Multiple risk factors have been linked to PM, but there is no consensus among authors. Age, diagnosis, cardiopulmonary status, the presence of pulmonary hypertension, infections, use of glucocorticoids and many others have been described in different studies individually, with no unanimity.

The purpose of this paper is to analyse mortality at 30 days after LT in a retrospective cohort and identify those risk factors that significantly condition mortality in COPD patients undergoing LT.

Materials and methods

A retrospective cohort of lung transplant patients and patients with COPD from the La Fe University and Polytechnic Hospital was analysed, ranging from the programme's beginning in 1991 until December 31st, 2008. The follow-up period was established to be from when the procedure was conducted until the patient's death or, for surviving patients, until the closing date of the study, January 1st, 2013.

The clinical diagnosis of COPD was defined by international guidelines[9] or according to those in force the time of diagnosis. All patients accepted for LT were included in the programme according to international criteria.[10]

The following preoperative variables of the patient were analysed, obtained at the time of their inclusion on the LT waiting list or when that data was updated closer to the surgical procedure: age, sex, height, weight, body mass index, diagnosis (COPD rather than deficit of alpha-1-antitrypsin), degree of dyspnoea *(Medical Research Council scale)*, *Body mass index, airflow Obstruction, Dyspnoea and Exercise capacity index* (BODE),[11] calculated retrospectively in transplant patients before 2004, smoking habit, pre-LT hospitalisations and intensive care admission, dependence on corticosteroid therapy (more than 10 mg/day of prednisone or equivalent) and bronchiectasis. The respiratory functional status of patients before LT was also analysed: forced vital capacity, forced expiratory volume in one second, forced expiratory flow 25–75%, diffusing capacity for carbon monoxide, in absolute terms (litres) and by percentage of the reference value, and the 6 min walk test measured in metres and with the percentage of reference value.

In regard to the donor, the variables of sex, age, height, weight and body mass index were included.

The analysed variables of surgical procedure were: LT (one or both lungs), use of extracorporeal circulation, characteristics of the retrograde perfusion of the graft – conducted during preparation for the transplant or prior to implant – time taken for ischaemia, need for blood transfusion and ratio of pressure arterial oxygen/fraction of inspired oxygen (PaO_2/FiO_2).

Primary graft dysfunction (PGD) after lung transplantation was defined when PaO_2/FiO_2 was <200 in the first 72 h after the LT.[12] After 2005, PGD failure was defined according to the international consensus of the *International Society for Heart and Lung Transplantation* (ISHLT), with the presence of pulmonary infiltrates in chest radiograph and a ratio of PaO_2/FiO_2 <300.[13]

PM was defined as that which occurred in the first 30 days after LT.

Statistical analysis

Continuous variables were expressed as a mean ± standard deviation. Categorical variables were expressed as absolute frequencies and percentages. The analysis and comparison of means were performed using the Student's *t* test, and to compare percentages the Chi^2 test or Fisher's test was used when appropriate. The Cox regression model, the *stepwise forward* method, was used for the multivariate analysis and this analysis included the variables that had shown a tendency to statistical significance in the univariate analysis ($p < 0.2$). The results were expressed using relative risk (RR) and the confidence interval was 95% (CI 95%). $p < 0.05$ was defined as statistically significant.

Results

A total of 107 patients underwent transplants with a mean survival rate of 2.36 years (CI 95% 1.26–3.46). The recipients' characteristics, both as the entire cohort and divided into subgroups, are detailed in Table 1.

Using the clinical and functional respiratory variables (body mass index, airflow obstruction, dyspnoea, exercise capacity) each