



Original Article

Lung Transplantation in Cystic Fibrosis and the Impact of Extracorporeal Circulation[☆]

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ABSTRACT

Introduction: Lung disease is the major cause of death among cystic fibrosis (CF) patients, affecting 80% of the population. The impact of extracorporeal circulation (ECC) during transplantation has not been fully clarified. This study aimed to evaluate the outcomes of lung transplantation for CF in a single center, and to assess the impact of ECC on survival.

Methods: We performed a retrospective observational study of all transplanted CF patients in a single center between 1992 and 2011. During this period, 64 lung transplantations for CF were performed.

Results: Five- and 10-year survival of transplanted patients was 56.7% and 41.3%, respectively. Pre-transplantation supplemental oxygen requirements and non-invasive mechanical ventilation (NIMV) do not seem to affect survival ($P=0.44$ and $P=0.63$, respectively). Five- and 10-year survival among patients who did not undergo ECC during transplantation was 75.69% and 49.06%, respectively, while in those who did undergo ECC during the procedure, 5- and 10-year survival was 34.14% and 29.87%, respectively ($P=0.001$). PaCO₂ is an independent risk factor for the need for ECC.

Conclusions: The survival rates of CF patients undergoing lung transplantation in our hospital are similar to those described in international registries. Survival is lower among patients receiving ECC during the procedure. PaCO₂ is a risk factor for the need for ECC during lung transplantation.

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El trasplante pulmonar en la fibrosis quística y la influencia de la circulación extracorpórea

RESUMEN

Introducción: La enfermedad pulmonar es la principal causa de mortalidad en el 80% de los pacientes con fibrosis quística (FQ). La influencia de la circulación extracorpórea (CEC) no está completamente establecida. Los objetivos son evaluar los resultados del trasplante pulmonar por FQ en un solo centro y la influencia de la CEC sobre la supervivencia de estos pacientes.

Métodos: Estudio observacional retrospectivo de todos los pacientes afectados de FQ trasplantados en un solo centro entre 1992 y 2011. En este período se han realizado 64 trasplantes pulmonares por FQ.

Resultados: La supervivencia de los pacientes trasplantados a los 5 y 10 años fue del 56,7 y el 41,3%, respectivamente. El requerimiento de oxígeno suplementario previo al trasplante no parece afectar a la supervivencia ($p=0,44$), al igual que los pacientes que se trasplantaron con ventilación mecánica no invasiva ($p=0,63$). La supervivencia a los 5 y 10 años para los pacientes que no se trasplantan con CEC es del 75,69 y el 49,06%, respectivamente, mientras que los que se trasplantan bajo CEC tienen una supervivencia a los 5 y 10 años del 34,14 y el 29,87%, respectivamente ($p=0,001$). La PaCO₂ es un factor de riesgo independiente para la necesidad de CEC.

Palabras clave:

Fibrosis quística

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Conclusiones: Los pacientes con FQ trasplantados pulmonares en nuestro centro tiene una supervivencia similar a la descrita por los registros internacionales. Los pacientes trasplantados bajo CEC tienen una menor supervivencia. La PaCO₂ es factor de riesgo de necesidad de CEC durante el trasplante pulmonar.

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Introduction

Cystic fibrosis (CF), which occurs in 1 out of 5500 births, is the most common genetic disease in Caucasians.¹

Lung disease is the main cause of death in 80% of patients and the only intervention that has been shown to improve the survival of patients with advanced lung disease is lung transplantation (LT).²

As sequential bilateral LT becomes more common and surgical techniques improve, the use of extracorporeal circulation (ECC) in LT has declined.

Studies that evaluate the impact of ECC in LT are limited to the most prevalent diseases: chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF).^{3,4}

The main objective of this study was to evaluate the LT outcomes in CF and long-term survival in a single center. Secondary objectives were to evaluate the impact of ECC on survival and to identify factors that may determine the need for this therapy.

Methods

This was a retrospective observational study conducted in all CF patients receiving lung transplants in the Hospital Vall d'Hebron (Barcelona, Spain) between April 1, 1992 and September 30, 2011. During that period, 64 LTs were performed for CF in our center.

Transplant recipients were followed up until September 2014, so the minimum follow-up, unless patients died earlier, was 3 years.

ECC was applied during the procedure at the discretion of the surgical team, according to the criteria listed below, previously published in the literature⁵:

1. Scheduled: for correction of cardiac defects during transplantation.
2. Technical difficulties during the surgical procedure: cardiac or pulmonary lesions, impossibility for lung collapse, etc.
3. Cardiac dysfunction and right ventricular failure.
4. Hyperacute graft dysfunction or pulmonary edema after implantation of the first lung.
5. Cardiac index <2 L/min/m².
6. Mixed venous oxygen saturation <60%.
7. Arterial oxygen saturation <85%.
8. Mean pulmonary artery pressure >50–60 mmHg.
9. pH<7.00.

Prolonged mechanical ventilation (MV) was defined as MV administered for more than 21 days.⁶

Absolute frequencies and percentages were used to describe nominal variables. Quantitative variables were compared using the χ^2 test or Fisher's test as needed. Survival was calculated using the Kaplan–Meier test. Since the probability of requiring ECC can differ among individuals and the factors that lead to the requirement of ECC may also affect survival, a propensity score analysis was used to control for the possibility of confounding factors.

Stata 13.1 software was used for the statistical analysis.

Results

Mean age was 20.7±8 (r: 9–49) years. Twenty-six (40.6%) patients were included in the pediatric LT program (0–17 years), with a mean age of 13.9 (r: 9–17) years. The other 38 patients were

from the adult LT program (18–49 years), with a mean age of 35.3 (r: 18–49) years.

Of the 64 LTs, 33 (51.5%) were male and 31 (48.5%) were female, yielding a male/female ratio of 1.06/1.

Mean body mass index (BMI) was 16.9±2.7 (r: 10–22.9) kg/m². According to the WHO classification,⁷ 25 patients had severe malnutrition.

Mean time on the waiting list was 9.3±8.5 (r: 0–34) months. For the pediatric transplant group, the mean wait was 9 (r: 0.7–34.7) months, and for the adult group it was 10.5 (r: 0.1–30.2) months.

With regard to oxygen needs prior to LT, 51 (79.6%) patients used chronic home oxygen therapy, and 13 (20.3%) patients required non-invasive mechanical ventilation (NIMV). Mean time using oxygen therapy before the LT was 15.9±21.4 (r: 1–96) months.

At the time of inclusion in the waiting list for LT, patients had median PaO₂ values of 63 (r: 27–85) mmHg and PaCO₂ 43.5 (r: 30–84) mmHg. Pulmonary function test (PFT) values (%) for FVC were 38.4±14 (r: 14–82) and FEV₁ 26±10 (r: 13–60). Mean distances on the 6-minute walk test (6MWT) were 323±111 (r: 72–636) m.

LT recipients received MV for a mean period of 10 days (r: 1–60 days). Twelve patients (18.7%) required prolonged MV. Mean intensive care unit (ICU) stay was 17.7±16.7 (r: 1–90) days.

Mean time to achieve best lung function was 41.1 (r: 1.7–167.5) months post-LT (Fig. 1).

The only variable identified in the univariate analysis that increased the probability of death was preoperative PaCO₂ (HR: 1.05; 95% CI: 1.02–1.09) (Table 1).

Actuarial survival (Kaplan–Meier) of patients transplanted for CF at 1, 3, 5, and 10 years was 71.8%, 62.4%, 56.7%, and 41.3%, respectively, with a median survival of 5.7 years. Patients were divided into 2 time periods: 1992–2002 and 2003–2011. Survival at 1, 3, 5,

Table 1

Univariate Analysis of Risk Factors for Mortality According to the Cox Proportional Hazards Method.

Variable	HR	95% CI	P-value
Age (years)	1.02	0.97–1.07	.526
BMI (kg/m ²)	0.99	0.88–1.12	.955
Waiting list time (months)	0.97	0.93–1.02	.261
PaO ₂ (mmHg)	0.99	0.96–1.03	.842
PaCO ₂ (mmHg)	1.05	1.02–1.09	.003
FVC prior to LT			
ml ^a	1	0.99–1	.851
% ^b	0.99	0.96–1.02	.561
FEV ₁ prior to LT			
ml ^a	1	0.99–1	.972
% ^b	0.99	0.95–1.03	.883
6MWT prior to LT (m)	1	0.99–1	.658
Hospitalizations in the last year	1.12	0.93–1.36	.228
Ischemia time (min)	1	0.99–1	.782
Time on MV (days)	1.01	0.98–1.03	.570
Time of ICU stay (days)	1	0.97–1.02	.984

6MWT: 6-minute walk test; 95% CI: 95% confidence interval; BMI: body mass index; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; HR: hazard ratio; PaO₂: partial pressure of oxygen; PaCO₂: partial pressure of carbon dioxide; VM: mechanical ventilation.

^a FVC and FEV₁ expressed in milliliters.

^b FVC and FEV₁ expressed as a percentage of the predicted value.

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