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Original Article

Effects of nutritional status and dietetic interventions on survival in Cystic Fibrosis patients before and after lung transplantation

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Abstract

Background: This study retrospectively investigated nutritional status, dietetic intervention and intake in Cystic Fibrosis (CF) patients before and after lung transplantation (LTX).
Methods: Body Mass Index (BMI), Fat Free Mass Index (FFMI) and nutritional intake were retrieved from 75 out-patients aged 15–53 years. Patients were seen every 3–4 months during the waiting list time (range 0–81 months) and up to 116 months after LTX. Survival was measured in months.
Results: The median BMI at baseline was 19.2 kg/m^2 (range: 15.3 to 28.4 kg/m^2) with 29 patients (39%) below ≤ 18.5 kg/m^2. FFMI (measured in 65 patients) had a median of 15.2 kg/m^2 (range: 11.1 to 22.4 kg/m^2) with 39 patients (60%) ≤ 16.7 kg/m^2 (men) or ≤ 14.6 kg/m^2 (women). Median energy intake was 2800 kcal, 239 kcal higher than the estimated energy requirement. However, 8 patients consumed ≥ 500 kcal less than recommended. Protein intake was 104 (range 60–187) g or 1.9 g/kg per day. Despite dietetic intervention with oral nutritional supplements (ONS) (36 patients), tube feeding (12 patients), or both (13 patients), BMI and FFMI hardly improved pre-LTX. LTX was performed in 51 patients (68%); 10 patients died during follow-up, median survival time was 41 months. A BMI ≤ 18.5 kg/m^2 was more prevalent in patients who died before LTX (6/9) or who died after LTX (4/10) than in patients who were still alive on the waiting list (5/15) or who survived LTX (14/41). Results for FFMI were comparable. From 6–12 months post-LTX, BMI and FFMI markedly improved, especially in underweight patients.
Conclusion: A BMI ≤ 18.5 kg/m^2 and an FFMI ≤ 16.7 kg/m^2 (men) or ≤ 14.6 kg/m^2 (women) appears to impair survival in LTX candidates with CF. Patients maintained a low body weight before LTX. After LTX weight gain is achieved.

Keywords: Cystic Fibrosis; Lung transplantation; Nutritional status; Nutritional intervention; Body Mass Index; Fat Free Mass

1. Introduction

Lung transplantation (LTX) is an established treatment option for end-stage lung disease in Cystic Fibrosis (CF) patients [1]. An optimal nutritional status pre-and post-lung transplant is an important predictor of survival in CF patients [2,3]. However, malnutrition is a common problem in patients with CF due to fat malabsorption and a higher energy expenditure as a result of inflammation, frequent periods of severe respiratory tract infections, and increased work of breathing when lung function declines [4,5]. A good indicator of nutritional status in CF

Abbreviations: AF, Activity Factor; BMI, Body Mass Index; CF, Cystic Fibrosis; CFRD, Cystic Fibrosis-Related Diabetes; FEV1, Forced Expiratory Volume in 1 s; FFM, Fat Free Mass; FFMI, Fat Free Mass Index; HU, High Urgency; LTX, Lung transplantation; ONS, Oral nutritional supplements; PEG, Percutaneous Endoscopic Gastrostomy; RMR, Resting Metabolic Rate; UMCU, University Medical Center Utrecht; WHO, World Health Organization.

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patients is Body Mass Index (BMI) [2,6]. Underweight adult CF patients (BMI < 18.5 kg/m^2) have a 25% higher risk of mortality than adult CF patients with a normal weight [7]. On the other hand, the prevalence of overweight and obesity in CF patients is increasing, with estimates ranging from 10% in the UK [8,9] to 18.4% in Canada. This may not be desirable, because mortality after LTX was shown to be higher in underweight, overweight, and obese patients (including CF patients) than in normal-weight patients [10]. A BMI below 18 kg/m^2 is often used as a preclusion for LTX [1]. Thus, keeping the BMI between 18 and 30 kg/m^2 before LTX is an important treatment goal.

Lean body mass or Fat Free Mass (FFM) is another indicator for nutritional status. It is a measure of muscle mass and correlates with (inspiratory) muscle function, quality of life [11], and lung function [12]. Depletion of FFM is strongly associated with increased mortality while awaiting LTX and with prolonged post-transplant intensive care unit stays [3]. This means that not just body weight but also FFM should be monitored in CF patients to avoid fat accumulation and loss of muscle mass.

Pre- and post-transplant nutrition management is aimed to maintain or improve nutritional status, in order to meet the criteria for LTX and optimize survival before and after LTX. Few studies have investigated nutritional intervention strategies in patients on the waiting list for lung transplantation [2,13,14]. One study demonstrated that Percutaneous Endoscopic Gastrostomy (PEG) feeding may improve body weight before LTX in patients with a low BMI [2]. Another study showed that three appointments with a dietician were not sufficient to improve nutritional status in underweight lung transplant candidates [13]. An intensive nutritional programme with extra meals and nutritional supplements during hospitalization in underweight patients with end-stage lung disease was effective in increasing energy intake and body weight compared to regular nutritional support [14]. Until now, insight into the nutritional status and the effect of dietetic intervention in pre- and post-transplant CF patients is limited. Therefore, the aim of this study was to describe nutritional status and intake at waiting list entry, subsequent changes in body weight and FFM before and after LTX, and survival after LTX using data from out-patient visits.

2. Methods

2.1. Study design

2.1.1. Data at waiting list entry (n = 75 patients)

In the period August 1998–June 2011, 110 CF patients from different CF centres in the Netherlands had been screened for LTX. Of these, 98 patients were accepted on the waiting list but we could retrieve data from 75 CF patients (aged ≥ 15 years) from our own patient files. All LTX transplants were performed in the Lung Transplantation Center, University Medical Center Utrecht.

2.1.2. Follow-up data (31 of 75 patients)

Of the 75 patients, 51 had an LTX. Unfortunately complete follow-up data on anthropometry and diet were only available for 31 of these patients: 10 died after LTX and 10 patients were followed for less than 1 year. For the remaining 31 patients we retrieved anthropometric data at four time points: (1) waiting list entry (baseline); (2) last outpatient visit pre-LTX; (3) 6–12 months outpatient visit post-LTX and (4) 18–24 months outpatient visit post-LTX. Time between the waiting list entry and LTX ranged between 0 and 81 months. Because no nutritional data were available for the moment of LTX, we chose the 'last outpatient visit pre-LTX' for time point 2.

2.1.3. Nutritional management

Dietetic care was provided by two registered dieticians to maintain or improve nutritional status before and after LTX. During a dietetic consultation patients' nutritional status, dietary requirements, and dietary intake (from a dietary history) were assessed. If necessary, use of additional ONS and/or tube feeding was advised or maintained. Patients were seen as out-patients every 3–4 months. When patients were unable to maintain body weight, the daily use of ONS was increased, tube feeding was started, or the type of tube feeding was changed from normal (1.5 kcal/ml) to energy enriched (2 kcal/ml). These adjustments were individual and therefore, they are not reported in this paper. None of the patients used appetite stimulants.

2.1.4. Clinical measurements

Medical, anthropometric, and nutritional characteristics were determined at baseline and subsequently every 3–4 months when the patient had been admitted to the waiting list. After LTX the patients were seen in the outpatient clinic every three months the first year, every six months the second year and once a year after three years.

2.1.5. Medical characteristics

Patient data and surgery-related characteristics were extracted from electronic medical records.

Pulmonary function was assessed by spirometry (ZAN; Oberthulba, Germany) and expressed as FEV1% of the predicted normal Forced Expiratory Volume in 1 s (FEV1). All FEV1 measurements were performed by the Laboratory for lung function of the UMCU. *Cystic Fibrosis-Related Diabetes (CFRD)* was recorded because of its negative effect on lung function, particularly in women [15]. Diagnosis of CFRD was based on the criteria proposed by the American Diabetes Association 2011 [16].

Pancreatic insufficiency was defined as having insufficient pancreatic function to achieve normal intestinal absorption of fat, therefore requiring pancreatic enzyme replacement therapy (PERT) from an early age.

A *High Urgency (HU) status* was assigned to patients whose life expectancy was estimated to be less than three months according to Eurotransplant guidelines [17].

2.1.6. Anthropometric characteristics

BMI was classified according to the WHO recommendations [18] and the European Consensus Report for CF [19]: underweight ≤ 18.5 kg/m^2; normal weight 18.5–24.9 kg/m^2 and overweight 25–29.9 kg/m^2. For the 8 adolescents (< 18 years)