



Weight Gain and Acute Rejection in Patients Submitted to Pulmonary Transplantation: A Retrospective Cohort of 10 Years

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ABSTRACT

Objective. Acute rejection is one of the most common complications after pulmonary transplantation. The aim of this work was to verify the association of nutritional status and weight gain with acute rejection in the recipient during the 1st year after pulmonary transplantation.

Methods. Retrospective cohort study with patients submitted to pulmonary transplantation at a pulmonary transplantation center in the state of São Paulo. Data on sex, age, underlying disease, type of transplantation, and presence, degree, and frequency of rejection according to the transbronchial biopsy results were collected, along with body mass index (BMI) and weight variation over the course of 1 year. The difference between groups was analyzed by means of Student *t* test and the association by means of chi-square test. Significance was considered with $P < .05$.

Results. A total of 117 patients were included, of which 71 (60.7%) were male. The average age was 39.8 ± 15.5 years. There were 77.8% with acute rejection in the 1st year after transplantation. The nutritional status of eutrophy prevailed according to BMI in both adolescents and adults, with no association with acute rejection ($P = .80$), and there was a greater weight gain among the individuals who showed rejection, with an increase of 7.58 kg (95% confidence interval [CI] 6.35–8.81) compared with those who did not present rejection, whose average weight gain was 4.12 kg (95% CI 1.28–6.95; $P = .01$).

Conclusions. Nutritional status was not associated with acute cell rejection in the 1st year after transplantation, although weight gain was greater in those who had rejection.

ACUTE rejection is one of the most common complications after lung transplantation, a treatment option for patients with advanced pneumopathy diseases unresponsive to conventional drug therapies, promoting increased expectation and improved quality of life [1,2]. The most frequent rejection is acute cell rejection, characterized by mononuclear perivascular and interstitial cell infiltration [3]. It occurs more frequently in the 1st 6 months after pulmonary transplantation [4]. The diagnosis is made with the use of transbronchial biopsy, the primary method of diagnosis of acute cell rejection, routinely requested independently from patient's symptoms, throughout the 1st year after transplantation [5,6].

Obesity and malnutrition are independent risk factors that contribute to mortality in the period after pulmonary transplantation, accounting for up to 12% of deaths in the 1st year [7]. The body mass index (BMI) has been accepted as a useful tool to evaluate the nutritional status of patients who are waiting for pulmonary transplantation. It was

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shown to be able to predict unfavorable postoperative evolution by pointing that patients with BMI $<17 \text{ kg/m}^2$ or $>27 \text{ kg/m}^2$ before transplantation had a higher mortality in the 1st 90 days after transplantation [8].

Currently, little is known about the relationship between nutritional status and weight gain with acute rejection. Therefore, the present study aimed to verify the association of nutritional status and weight gain with acute rejection in the recipient during the 1st year after pulmonary transplantation.

METHODS

Population Under Study

A retrospective analysis was carried out of 191 patient charts of patients of both sexes submitted to lung transplantation from August 2003 to September 2013 at the Pulmonary Transplantation Center of the Heart Institute (InCor), Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, Brazil.

Data Acquisition

The data were obtained from an electronic chart and/or database from the InCor Pulmonary Transplant Team. The variables collected included sex, age, underlying disease, type of transplantation, and presence, degree, and frequency of acute cell rejection.

Underlying pulmonary diseases were classified into 4 diagnostic groups: suppurative (cystic fibrosis and bronchiectasis), obstructive (emphysema and bronchiolitis), restrictive (pulmonary fibrosis and idiopathic pulmonary fibrosis), and other (pulmonary lymphangiomyomatosis, pulmonary microlithiasis, silicosis, histiocytosis X, sarcoidosis) diseases. Two types of transplantations were performed: unilateral right or left and bilateral.

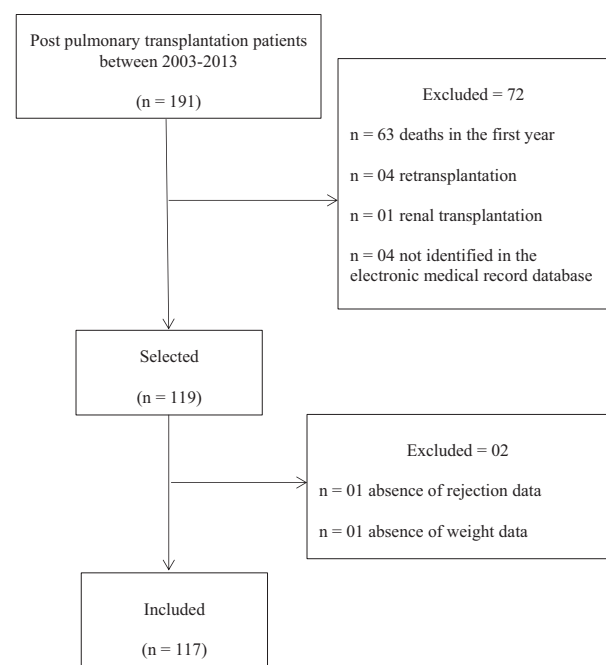


Fig 1. Flowchart of the studied patients.

Table 1. Baseline Characteristics of Lung Transplantation Recipients 2003–2013 (n = 117)

Characteristic	n (%)
Male sex	71 (60.7%)
Age, y (mean \pm SD)	39.8 \pm 15.5
Bilateral transplant	96 (82%)
Underlying disease	
Suppurative	65 (55.6%)
Obstructive	25 (21.4%)
Restrictive	17 (14.5%)
Other	10 (8.5%)

All patients, in the 1st year after transplantation, underwent surveillance bronchoscopy at 6 different times (2nd and 6th weeks and 3rd, 6th, 9th, and 12th months), subject to changes according to the patient's clinical status at each time. The transbronchial biopsy was used to verify the presence or absence of acute rejection and the classification according to the International Society for Heart and Lung Transplantation (A0, no rejection; A1, minimal rejection; A2, mild rejection; A3, moderate rejection; A4, severe rejection) according to the intensity of the perivascular mononuclear infiltrate in the lung parenchyma [9]. In the case of >1 episode of rejection, the most severe rejection during the year was considered, and for analysis of the association with nutritional status and weight gain, biopsies were considered from the 6th week of transplantation on.

In the 1st year, all patients received the following therapy: 40 g/d prednisone while in the hospital period, followed by reduction by 5 mg every week after hospital discharge until reaching 20 g/d maintained until the 6th month, when further reduction was performed until the maintenance dose of 5 g/d was reached. In the presence of \geq A2 rejection, a patient received 10 mg/kg/d methylprednisolone pulse therapy for 3 days and then a new therapy of prednisone decreasing from 40 g/d to 5 g/d.

Weight and height were obtained at the outpatient visits in the 1st year after the transplantation. The data after the 6th week of transplantation were included, because by that time patients have usually passed the most critical postoperative phase.

The BMI was calculated using the formula: weight (kg) \div [height (m)]², considering, in the calculation, the highest weight of the patient in the period. The nutritional status of adolescents (<20 y of age) [10] was classified by the percentile of the BMI curve for age as malnutrition (<5 th percentile), eutrophia (5th to <85 th percentile), overweight (85th to <95 th percentile), and obesity (≥ 95 th percentile). For adults (20 to <60 y of age) [11], malnutrition was indicated by BMI $<18.5 \text{ kg/m}^2$, eutrophia by BMI 18.5 to $<25 \text{ kg/m}^2$, overweight by BMI 25 to $<30 \text{ kg/m}^2$, and obesity by BMI $\geq 30.00 \text{ kg/m}^2$; and for the elderly (≥ 60 years) [12], the

Table 2. Distribution of Patients According to the Degree of Acute Cellular Rejection in the 1st Year After Pulmonary Transplantation (n = 117)

Degree of Acute Cellular Rejection	n (%)
A0	12 (10.3%)
A1	29 (24.8%)
A2	68 (58.1%)
A3	08 (6.8%)
A4	–

Abbreviations: A0, no rejection; A1, minimal rejection; A2, mild rejection; A3, moderate rejection; A4, severe rejection.

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