Original Article

Optimization of nutritional management of patients awaiting lung transplant at the Strasbourg University Hospitals

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SUMMARY

Background & aims: Lung transplantation represents a key treatment option for patients with chronic respiratory failure. Nutritional status and management appear to have a major impact on post-transplant outcome. The recommendations of the French-Speaking Society of Clinical Nutrition and Metabolism (SFNEP) are reference guidelines for managing undernutrition. The aims of this study were to provide an insight into the pre- and post-lung transplant nutritional status and nutritional management of these patients.
Methods: This was a single-center, retrospective, comparative, observational study, which was focused on patients who were the most at risk for undernutrition or worsening of preexisting undernutrition. We included patients with BMIs of less than 25 kg/m^2 at pre-transplant evaluation. We collected general and nutritional data during the follow-up of our patients before and after transplantation.

Results: We included 62 patients aged $\geq$18 years who had undergone lung transplantation between January 1, 2012 and December 31, 2015 at the university hospitals of Strasbourg. During the pre-transplant evaluation and in the immediate post-transplant period, the observed enteral nutrition rate was significantly lower compared to the SFNEP recommendations (respectively odds ratio [OR] = 0.18 [0.06–0.58], p = 0.004 and OR = 0.15 [0.05–0.40], p < 0.001). We thus observed a strong decrease in BMI following lung transplant and during the transplant continuing care unit stay (19.9 $\pm$ 2.8 kg/m^2 before transplantation vs 17.8 $\pm$ 2.5 kg/m^2 after the intensive care unit hospitalization). The mean duration until weight loss could be corrected and pre-transplant BMI re-attained was 1 year. The median hospitalization duration wasn't significantly longer in patients with BMI >21 kg/m^2 compared to patients with BMI $\leq$21 kg/m^2 (43.5 vs 39 days, p: 0.487). We also determined that ensuring a BMI of 22.8 kg/m^2 before the transplantation could limit the risk of a fall in BMI below 21 kg/m^2.

Conclusions: This study demonstrated how important a role nutritional management plays starting from pre-transplant evaluation, with the goal of reaching a target BMI to prevent undernutrition wherever possible.

1. Introduction

Lung transplantation has become a major option for patients with end-stage chronic respiratory failure. Nutritional status and management appear to have an impact on post-transplant outcome. Undernutrition is an ubiquitous phenomenon in respiratory diseases [1–5], both in patients who have been transplanted or are awaiting transplantation.

Following major surgery, undernutrition exposes patients to the risk of amyotrophy [6], loss of autonomy, and increased mean hospital stay duration [7,8]. A study reported that patients with undernutrition had 53% higher risk of developing a nosocomial infection, and those with severe malnutrition a 302% higher risk, compared to patients without undernutrition [9].

The recommendations of the French-Speaking Society of Clinical Nutrition and Metabolism (SFNEP) [10] are reference guidelines for managing undernutrition. The SFNEP gave definitions for moderate and severe undernutrition, based on clinical and biological criteria in patients aged <70 years (Table 1) [10] and published a decision tree for their management according to severity (Fig. 1) [11].

Mild undernutrition is not clearly defined except in the following French Health Authority (HAS) definition: "(…) weight loss results in a weight below minus one standard deviation or more, but less than two, from the mean value for the reference population. When only one measurement is available, there is a strong presumption of mild undernutrition when the measured weight is below minus one standard deviation or more, but less than two, from the mean value for the reference population." [12].

Dieticians refer to the SFNEP decision tree for prescribing oral nutritional supplements (ONS) or artificial nutrition. One drawback of this tool is that it does not distinguish between the pathologies and surgical interventions of undernourished patients.

Previous studies on nutritional status and lung transplantation have mainly focused on overall weight evolution [13,14], consequences, complications, and mortality [15–19], but not helped define the optimal nutritional management for undernourished patients.

Table 1

Clinical and biological criteria corresponding to a moderate or severe undernutrition in patients aged <70 years according to the French-Speaking Society of Clinical Nutrition and Metabolism (SFNEP) [10].

Aged <70 years	Moderate undernutrition	Severe undernutrition
Weight loss		
Within 1 month	5—10%	≥10%
Within 6 months	10—15%	≥15%
BMI (kg/m^2)	≤18.5	≤16
Albumin	<30 g/L[a]	<20 g/L[a]
Transthyretin	<0.11 g/L	<0.05 g/L

BMI = body mass index (weight [kg]/size [m^2]).

[a] The inflammatory status must be considered when interpreting the albumin blood level.

Moreover, a BMI threshold for undernutrition has not been clearly defined for patients presenting with relative or temporary contraindications regarding the placement on lung transplant list, such as "limited functional status with poor rehabilitation potential" [20], whereas a threshold has been determined for severe obesity with a BMI >35 kg/m^2.

Our primary objective was to assess the impact of using the SFNEP decision tree for nutritional care on the management of patients awaiting lung transplant who are undernourished or at risk for undernutrition and on the initiation of enteral nutrition. The primary endpoint was the proportion of undernourished patients who received enteral nutrition as compared to the proportion who should have received this nutritional care according to the SFNEP criteria.

This study provides an insight into the pre- and post-lung transplant nutritional status and nutritional management, in order to make treatment proposals to optimize their nutritional management.

2. Materials and methods

This was a single-center, retrospective, comparative, observational study, which was focused on patients who were the most at risk for undernutrition or worsening of preexisting undernutrition. We included patients with BMIs of less than 25 kg/m^2 at pre-transplant evaluation. Overweight and obese patients were not included.
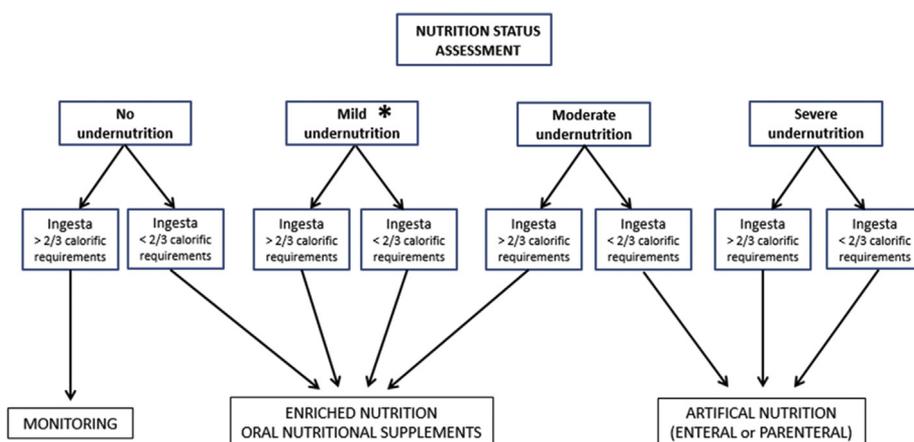
Fig. 1. Summary diagram based on the decision tree of the SFNEP [11]. Patient distribution according to their ingesta and SFNEP recommendations. Ingesta >2/3 and monitoring: n = 28; ingesta >2/3 and oral nutritional supplements: n = 16; ingesta >2/3 and artificial nutrition: n = 4. Ingesta <2/3 and monitoring: n = 0; ingesta <2/3 and oral nutritional supplements: n = 1, ingesta <2/3 and artificial nutrition: n = 13. (*) Recommendations not provided by the original SFNEP decision tree.

The patients' data was collected from the paper and computerized (using DxCare software) medical records, nursing records, dietary records (including nutritional disorder assessment sheets), pulmonary function testing (PFT) reports, and laboratory results server. Gender, age, pulmonary disease for which the patient was transplanted, date of transplantation, and albumin blood levels were recorded.

At the nutritional level, the following parameters were assessed: proportion of undernourished patients who received ONS and enteral nutrition; assessment of undernutrition severity according to the SFNEP reference guidelines (mild, moderate or severe) by one of the ward dieticians; BMI at pre-transplant evaluation, on the day before the intervention, and after the intervention (at 1 month, 3 months, 6 months, and 1 year); ingesta; change in BMI between the pre-transplant evaluation and the intervention, then between the intervention and day 28 post-intervention, with a detailed description of implemented nutritional management; percentage of post-intervention weight loss; efficacy of nutritional management, defined in our study as attaining BMI >21 kg/m^2 at 1 year post-transplant; hospital stay duration (Table 2). To perform the calculation of nutritional requirements, we used the Harris Benedict Equation. To calculate the nutritional intakes, we used the ANSES-CIQUAL food composition table.

Table 2
Summary table of patient data collected during the study.

	Pre-transplant evaluation	Immediate pre-operation	Immediate post-transplant (first month post-operation)	At 3 months post-transplant	At 6 months post-transplant	At 1-year post-transplant
Gender ratio	55% men 45% women					
Age (years)		55 ± 14				
Respiratory pathology causing the transplant	48% COPD 23% cystic fibrosis 13% pulmonary fibrosis 5% PAH 11% others					
Size (cm)	1.67 ± 10					
Weight (kg)	55 ± 13	56 ± 12	50 ± 10	52 ± 11	54 ± 12	56 ± 12
BMI (kg/m^2)	19.3 ± 2.9	19.9 ± 2.8	17.8 ± 2.5	18.3 ± 2.6	19.2 ± 2.7	19.8 ± 3
Albumin (g/l)	40.3 ± 5.3		32.9 ± 4.1			
% of need covered by ingesta	>**2/3**: 34% <**2/3**: 23% =**needs**: 43%		>**2/3**: 48% <**2/3**: 39% =**needs**: 13%			
SFNEP recommendations	- Monitoring: 45% - Enrichment and ONS: 28% - Artificial nutrition: 27%		- Monitoring: 8% - Enrichment and ONS: 31% - Artificial nutrition: 61%			
Undernutrition evaluation according to SFNEP reference guidelines	- No undernutrition: 39% - Mild undernutrition: 13% - Moderate undernutrition: 29% - Severe undernutrition: 19%		- No undernutrition: 3% - Mild undernutrition: 10% - Moderate undernutrition: 31% - Severe undernutrition: 56%			

Values are expressed as means. Ingesta evaluation: >2/3, at least 2/3 of the patient's needs covered by food intake; <2/3, less than 2/3 of the patient's needs covered by food intake, = needs: needs entirely covered by food intake. SFNEP recommendations depending on the patient's nutritional status: monitoring; dietary enrichment/ONS prescription; artificial nutrition: enteral nutrition using a gastrostomy tube or a nasogastric tube. BMI = body mass index (kg/m^2). COPD = chronic obstructive pulmonary disease. PAH = pulmonary arterial hypertension. ONS = oral nutritional supplements.

2.1. Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or median with interquartile range, depending on the normality of distribution. Categorical variables are presented as numbers and percentages. The observed rate of enteral nutrition and theoretical rate according to SFNEP recommendations were compared using a mixed logistic regression model with a random "patient" effect. Comparisons of secondary endpoints were performed in the same way. The results are presented as odds ratios (ORs) with their 95% confidence intervals (CIs). BMI evolution was modeled by two contiguous straight line pieces for each group (mild *vs*. severe undernutrition) using a linear mixed model. The results are presented as mean differences with their 95% CIs. We performed a receiver operating characteristic (ROC) curve analysis in order to assess the performance of BMI the day before the intervention for predicting the occurrence of undernutrition during the year following transplantation and to define a target BMI to be reached before the graft. A p-value <0.05 was considered statistically significant. All analyses were performed using R software Version 3.2.2. (R Core Team, 2015).

3. Results

Our study included 62 patients aged ≥18 years who had undergone bilateral lung transplantation between January 1, 2012 and December 31, 2015 at the University hospitals of Strasbourg and who had a BMI of less than 25 kg/m^2 during the pre-transplant evaluation. The indications for lung transplantation were COPD (48%), cystic fibrosis (23%), pulmonary fibrosis (13%), pulmonary arterial hypertension (PAH) (5%) and some others causes (11%). The main patient characteristics have been summarized in Table 2.

Before transplant, 18 patients in our lung transplant cohort (29%) [18.2—41.9] received parenteral nutrition and 13 patients after transplant (21.7%) [12.1—34.2]. None of these patients were included in our study.

During the immediate post-transplant nutritional follow-up, frequent and systematic management was adopted: weight measurement twice a week, daily assessment of dietary intake compared to caloric requirements with caloric and protein supplementation if necessary, adaptations of dietary intakes according to the patient's desire set sour to maximize intakes taking into account recommendations according to the clinical context.

3.1. Use of enteral nutrition and SFNEP recommendations

The primary objective of our study was to assess the use of enteral nutrition in the pre-transplant period. Of 62 patients, five (8%) had been prescribed enteral nutrition during the pre-transplant evaluation, using percutaneous endoscopic gastrostomy (PEG). According to the SFNEP decision tree for the management of undernutrition, 17 patients (27%) should theoretically have received enteral nutrition in the pre-transplant evaluation. The observed enteral nutrition rate was significantly lower compared to the SFNEP recommendations (odds ratio [OR] = 0.18 [0.06—0.58], p = 0.004). In the immediate post-transplant period, *i.e.* during the month hospitalized at the transplant continuing care unit, 13 patients out of 62 (21%) had received enteral nutrition (using PEG for 9 patients and nasogastric tube for 4 patients). According to SFNEP decision tree for the management of undernutrition, 37 patients (61%) should theoretically have received enteral nutrition in the immediate post-transplant period (OR = 0.15 [0.05—0.40], p < 0.001). There was again a significant difference between the actual enteral nutrition rate and the recommendations during the month following lung transplant.

3.2. Assessment of oral dietary intake

At pre-transplant evaluation, 34% of patients had oral intake exceeding the two-thirds of their calorific requirements, 23% had oral intake below the two-thirds, and 43% had oral intake that satisfied their requirements.

During the immediate post-transplant month, 48% of patients had oral intake exceeding the two-thirds of their calorific requirements, 39% had oral intake below the two-thirds, and 13% had oral intake that satisfied their requirements. We recorded the total oral intakes and calories before and during intensive care post-transplant.

3.3. Evolution of albumin blood level

Albumin blood level is considered normal between 35 and 50 g/L. In the study population, the mean albumin level was 40.2 ± 5.3 g/L during pre-transplant evaluation and 32.9 ± 4.1 g/L in the immediate post-transplant period ($p < 0.001$). Thus, albumin blood levels decreased from the first days following transplantation.

3.4. Use of oral supplementation and SFNEP recommendations

We assessed the use of ONS in all their forms before and after lung transplantation. The prescription of ONSs was not standard but established after a specific evaluation of every patient nutritional requirements. When a patient refused to receive ONS, he was considered as not taking ONS, but the compliance remained satisfying. During pre-transplant evaluation, 45/62 patients (73%) had received oral supplementations. According to the SFNEP decision tree for the management of undernutrition, 17 patients (28%) should theoretically have received oral supplementations (OR = 0.11 [0.04–0.26], $p < 0.001$). The use of ONS was thus significantly higher than the SFNEP recommendations.

In the immediate post-transplant period (during hospitalization at the transplant continuing care unit), 53/62 patients (87%) had received oral supplementations. According to the SFNEP decision tree, 19 patients (31%) should theoretically have received oral supplementations (OR = 0.07 [0.03–0.17], $p < 0.001$). The use of ONS was thus significantly higher than the SFNEP recommendations.

At 3 months post-transplant, 38 patients (61%) were prescribed an ONS. At 6 months post-transplant, 28 patients (42%) were taking ONS. At 1-year post-transplant, 21 patients (33%) were still using ONS.

3.5. Changes in BMI before and after transplantation

We monitored the evolution of our patients' BMIs, calculated at the time of transplantation, upon discharge from the transplant continuing care unit, and at several time points following transplantation (1 month, 3 months, 6 months, and 1 year). All the patients who were followed up during the study received appropriate dietary advice (importance of protein intake, of maintaining muscle mass, etc.), possibly in association with ONS and enteral nutrition prescription. The pre-transplant mean weight was 55 ± 13 kg, corresponding to a BMI of 19.3 ± 2.9 kg/m^2, when nutritional management was initiated. The mean weight was 56 ± 12 kg the day before transplantation, corresponding to a BMI of 19.9 ± 2.8 kg/m^2. We observed a weight gain of 3.3%, i.e. 0.6 kg/m^2 BMI improvement, between patients' pre-transplant weight and that measured the day before transplantation. In the immediate post-transplant period, after the intensive care unit (ICU) hospitalization, the mean weight decreased to 50 ± 10 kg, corresponding to a BMI of 17.8 ± 2.5 kg/m^2. The mean weight was 52 ± 11 kg (BMI of 18.3 ± 2.6 kg/m^2) at 3 months post-transplant, 54 ± 12 kg (BMI of 19.2 ± 2.7 kg/m^2) at 6 months post-transplant, and 56 ± 12 kg (BMI of 19.8 ± 3 kg/m^2) at 1-year post-transplant (Table 2).

Between the day before transplantation and discharge from the transplant continuing care unit, the change in BMI was -9.7%, corresponding to a decrease of 1.9 kg/m^2. At 3 months post-transplant, the change was -6.9%, corresponding to a decrease of 1.4 kg/m^2. At 6 months post-transplant, it was -2.4%, corresponding to a decrease of 0.6 kg/m^2. At 1-year post-transplant, it was 0.9%, corresponding to an increase of 0.1 kg/m^2. We thus observed a strong decrease in BMI following lung transplant and during the transplant continuing care unit stay. The mean duration until weight loss could be corrected and pre-transplant BMI re-attained was 1 year.

According to the SFNEP reference guidelines, we realized an assessment of undernutrition severity. In the pre-transplant phase, only 24 patients (39%) were not undernourished, while eight (13%) exhibited mild undernutrition, 18 (29%) moderate undernutrition, and 12 (19%) severe undernutrition.

After post-transplant ICU hospitalization, two patients (3%) exhibited no undernutrition, six (10%) mild undernutrition, 19 (31%) moderate undernutrition, and 34 (56%) severe undernutrition (post-transplant data missing for one patient).

Body mass index evolution over time was also compared according to undernutrition severity at immediate post-transplant evaluation, with the patients divided into two groups: those with BMI >21 kg/m^2 ("mild" group: 8 patients) and those with BMI ≤21 kg/m^2 ("severe" group: 53 patients) (one missing data). We selected this threshold based on the one used in the BODE index to predict the risk of mortality in COPD patients (Table 3). The undernutrition thresholds determined by the SFNEP are valid for the general population. We wanted to have a more appropriate threshold for our population of patient with end-stage chronic respiratory failure. We observed a similar BMI evolution pattern in both groups, consisting in a marked decrease after transplantation, followed by a slow and gradual increase until a BMI close to the pre-transplant value was reached. During the weight loss phase, the difference in BMI variation slope between both groups was 0.68 kg/m^2 ([-0.25; 1.61], p = 0.359). During the recovery phase, the difference in slope was 0.03 kg/m^2 ([-0.06; 0.12], p = 0.885). At 1-year post-transplant, the difference in BMI between the groups was estimated at 3.70 kg/m^2 ([2.53; 4.86], p = 0.001) in favor of the "mild" group. This result also highlighted the importance of achieving an optimal BMI value before transplantation (Fig. 2).

3.6. Estimation of the "ideal" BMI to be reached before transplantation to avoid undernutrition

A theoretical "ideal" BMI to be reached the day before the intervention was determined to avoid the occurrence of undernutrition, defined in our study as a fall in BMI below 21 kg/m^2. We determined this theoretical ideal BMI, to be the closest to clinical reality. The aim was to optimize nutritional management so as to reach a minimal pre-transplant BMI that would remain above 21 kg/m^2, in the immediate post-transplant period, at 3 months, 6 months, and 1-year post-transplant. The ROC curve analysis showed an area under the curve (AUC) of 94.51 ([89.35; 99.67], p < 0.01) (Fig. 3). The chosen target BMI threshold was 22.8 kg/m^2, presenting a sensitivity of 80% and a specificity of 98%.

3.7. Assessment of hospitalization duration according to BMI

We assessed the impact of BMI on the hospitalization duration in the transplant continuing care unit for our patients with lung transplant. The study population was divided into two groups according the patients' nutritional status, with the "mild" group consisting of patients with BMI >21 kg/m^2 (8 patients) and the "severe" group consisting of patients with BMI ≤21 kg/m^2 (53 patients). There was no significant difference between both groups, with a median hospitalization duration of 43.5 [36.8—46.3] days for the "mild" group and 39 days [33.0—47.0] for the "severe" group (p = 0.487) (Fig. 4).

4. Discussion

Undernutrition, which results from insufficient energy and protein intake or hypercatabolism, is an ubiquitous phenomenon in respiratory diseases [1—5], both in patients who have been transplanted or are awaiting transplantation, as well as in those with cystic fibrosis [21—23]. The nutritional

Table 3
Variables and point values used to compute the BODE index.

| Variable	Points of BODE index			
	0	1	2	3
FEV1 of % predicted	≥65	50—64	36—49	≤35
6 MWD (m)	≥350	250—349	150—249	≤149
MMRC Dyspnea scale	0—1	2	3	4
BMI (kg/m^2)	>21	≤21		

Abbreviations: BMI, body mass index; BODE, Body mass index, degree of airway obstruction, Dyspnea and exercise capacity; FEV1, forced expiratory volume in 1 s; MMRC: Modified Medical Research Council; 6MWD, 6-min walk distance.
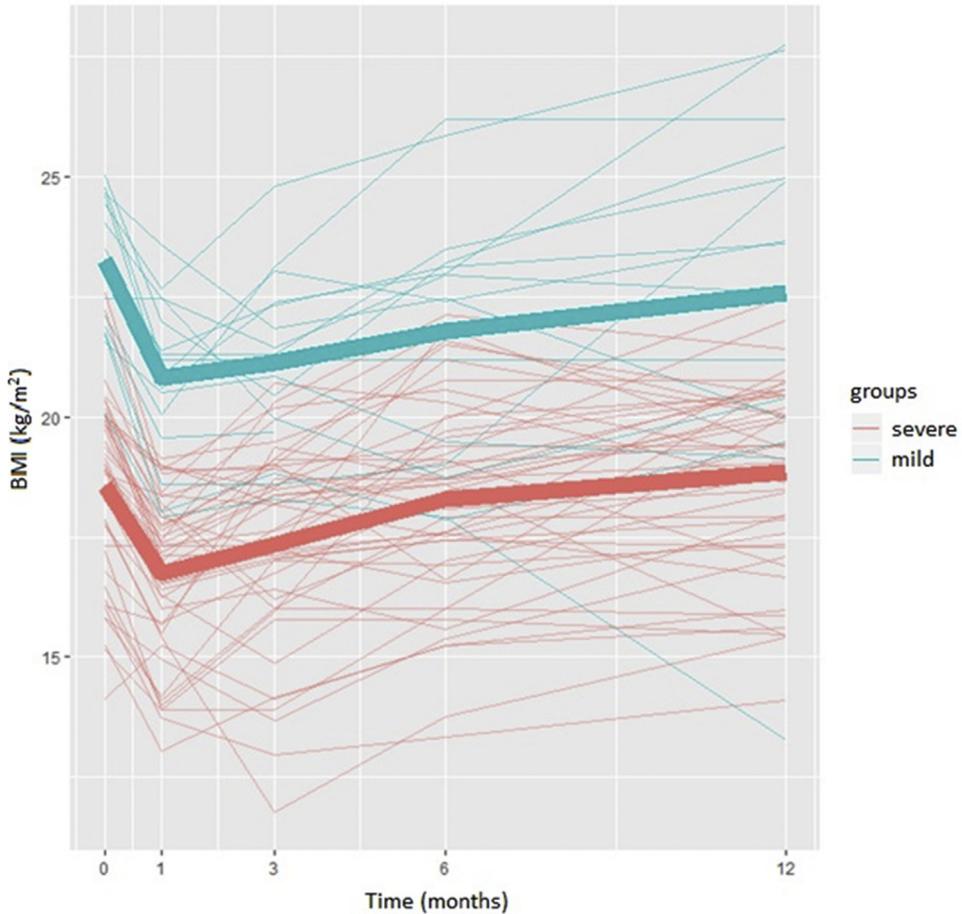
Fig. 2. Follow-up of BMI evolution over time according to undernutrition severity of patients included. "Mild" group: patients with BMI >21 kg/m^2 after pre-transplant evaluation. **"Severe" group:** patients with BMI ≤21 kg/m^2 after pre-transplant evaluation. Follow-up began immediately after lung transplant. We observed a similar BMI evolution pattern in both groups, consisting in a marked decrease after transplantation, followed by a slow and gradual increase until a BMI close to the pre-transplant value was reached. During the weight loss phase, the difference in BMI variation slope between both groups was 0.68 kg/m^2 ([-0.25; 1.61], p = 0.359). During the recovery phase, the difference in slope was 0.03 kg/m^2 ([-0.06; 0.12], p = 0.885). At 1-year post-transplant, the difference in BMI between the groups was estimated at 3.70 kg/m^2 ([2.53; 4.86], p < 0.001) in favor of the "mild" group.

management of post-lung transplantation patients plays a crucial role. According to the 26th report of the International Society for Heart & Lung Transplantation (ISHLT) [20], the main factors associated with mortality include primary graft dysfunction and infections during the first 30 days following lung transplantation, as well as chronic lung allograft dysfunction and infections during the 1st year. These patients need intensified nutritional management in order to improve their chances of early rehabilitation and decrease their risk of infection.

The BMI is divided into four categories: <18.5 kg/m^2: underweight, 18.5—24.9 kg/m^2: normal weight, 25—29.9 kg/m^2: overweight and ≥30 kg/m^2: obesity. In our study, we used these categories to assess the nutritional management of our patients, with a focus on the prescription of ONS and enteral nutrition in patients awaiting lung transplant with a BMI <25 kg/m^2. We noticed that during the pre-transplant and immediate post-transplant evaluations, enteral nutrition was insufficiently prescribed compared to the SFNEP recommendations, while the use of oral supplementation was significantly higher. Some reasons to explain why the SFNEP guidelines were not followed were patient refusal (e.g.
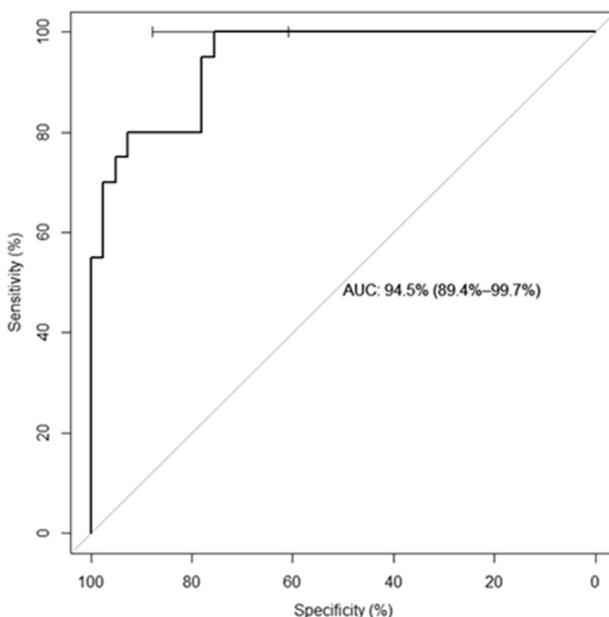
Fig. 3. Determination of the BMI threshold to be reached during the pre-transplant follow-up in order to prevent under-nutrition following transplantation, defined as a BMI < 21 kg/m^2. The efficacy of nutritional care was evaluated using a ROC curve, allowing us to determine a BMI threshold of 22.8 kg/m^2. This threshold has a sensitivity of 80% and a specificity of 98% [91.4; 100]. This means that patients with a BMI ≥22.8 kg/m^2 the day before the operation had a very low risk of having their BMI decrease below 21 kg/m^2 during the post-transplant follow-up period. AUC: area under the curve.

overestimation of his own nutritional intakes, physical or mental weariness) or digestive problems (gastroparesis, diarrhea). The use of ONS was sometimes easier to accept for some patients.

Despite this intensive oral supplementation, we observed a very marked immediate post-transplant BMI loss, and the mean duration until re-attaining the pre-transplant BMI was 1 year. Post-transplant undernutrition seems to be inescapable. In addition to hypercatabolism in continuing care services following major surgery, these patients also receive an extensive anti-rejection treatment that may have a major impact on intestinal absorption. We believe enteral nutrition should thus be employed more frequently to reduce the risk of undernutrition after transplant, especially PEG in the severely malnourished patient, allowing a more comfortable use than nasogastric tube.

Furthermore, resuming oral nutrition in an appropriate and sufficient way remains the top priority in the nutritional management of these patients. The use of enteral nutrition has an impact on the digestive tract and may lower oral intake.

After the initial weight loss, the gradual increase in BMI occurred through nutritional measures, associated with a resumption of physical activity. After transplant, we didn't use a balance with electric impedance, due to the many confounding factors that could hinder the interpretation of the results (presence of chest tubes, edema...). It therefore appears in our opinion to correspond to a real increase in muscle mass, not only in fat body mass.

Optimum and individualized nutritional management thus appears indispensable upon pre-transplant evaluation. Immediate post-transplant uses of systemic oral supplementation associated with an appropriate and individualized nutritional counseling is therefore probably advisable when patients do not receive enteral nutrition, given the initial muscle mass loss caused by bed rest, hypercatabolism, and wound healing. These results should also encourage us to make a patient more aware when he is at risk of malnutrition problem, as well as his family but also all the medical and paramedic staff involved in his care.
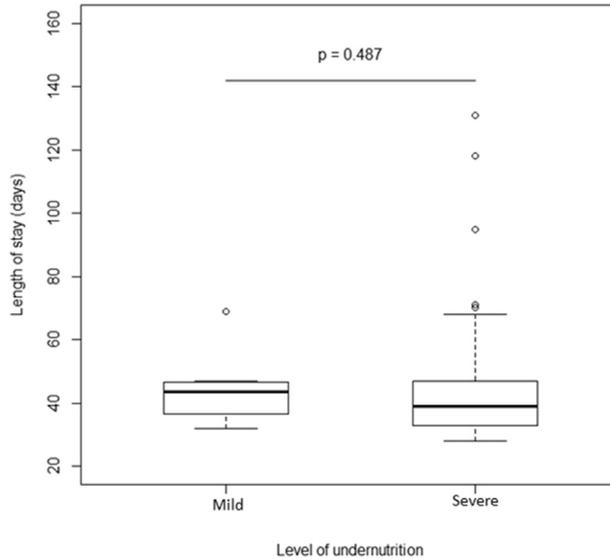
Fig. 4. Post-transplant hospitalization duration according to undernutrition severity. "Mild group": patients with BMI >21 kg/m^2 (8 patients). "Severe" group: patients with BMI ≤21 kg/m^2 (53 patients) (one missing data). There was no significant difference between both groups, with a median hospitalization duration of 43.5 [36.8—46.3] days for the "mild" group and 39 days [33.0—47.0] for the "severe" group (p = 0.487).

Another reason could explain the significant loss of weight in many patients despite our nutritional care. To assess their nutritional status and determine their nutritional management, we employed the undernutrition thresholds used for the general population but which appear not to be suitable for patients with severe respiratory failure. Some studies showed that COPD patients with a BMI <21.75 kg/m^2 had an increased risk of death [24]. In cystic fibrosis patients, the current ESPEN recommendations define an adequate nutritional status with a BMI ≥22 kg/m^2 for women and ≥23 kg/m^2 for men, even if a focus on BMI target alone not fully define nutritional status [25]. For these reasons, we also evaluated the severity of the malnutrition of our patients cohort using a more severe BMI threshold: 21 kg/m^2. We selected this threshold based on the one used in the BODE index (COPD was the respiratory pathology causing the transplant in 48% of the patients). This choice appears to us to be more relevant. Ideally, it would have been better to select a specific target BMI for each category of our patients according to the cause of transplant.

The study population was then divided into two groups: the "mild" group consisting of patients with BMI >21 kg/m^2 and the "severe" group consisting of patients with BMI ≤21 kg/m^2. We found that the BMI evolution after transplantation was significantly better in the "mild" group. But there wasn't any significant difference in the length of hospitalization after transplantation between the two groups.

We also determined an optimal target BMI to be reached before transplant in order to prevent post-surgery undernutrition (defined in our study as a fall in BMI below 21 kg/m^2), finding that ensuring a BMI of 22.8 kg/m^2 before the intervention could limit the post-transplant undernutrition risk. This value seems appropriate to optimally adjust nutritional management.

The SFNEP decision tree provides recommendations for the management of actual undernutrition at a given time, yet not for preventing potential weight loss. Given the risk of potential post-transplant weight loss, the dietician must anticipate and intensify the pre-transplant and immediate post-transplant nutritional management before undernutrition can occur. This study demonstrated that the vast majority of patients without initial undernutrition presented undernutrition following transplantation. Nevertheless, these results must be confirmed in a larger study population. A multi-center prospective study could allow validating the theoretical target BMI to be reached before transplantation, ideally for each category of pulmonary disease for which the patient was transplanted.

It should be noted that this study presents some limitations, notably its retrospective and single-center nature, as well as the limited number of patients included. We only selected patients with a pre-transplant BMI $\leq$25 kg/m^2. Overweight or obese patients were not included, although they too can be subject to considerable weight loss or undernutrition. We must also remain careful about some results: we didn't have analyzed other reasons for the high length of stay like infectious complications and we didn't have gathered some frequent digestive complications in post lung transplant patients, as gastroparesis.

In conclusion, we confirmed that individualized and efficient nutritional management in lung transplant candidates is essential. Our study demonstrated how important a role pre-surgery nutritional management plays starting from pre-transplant evaluation, with the goal of reaching a target BMI to prevent undernutrition wherever possible. According to previous studies and the current ISHLT recommendations, lung transplantation is formally contraindicated in patients with severe obesity (BMI>35 kg/m^2), yet patients with undernutrition also represent a major challenge which should not be underestimated.

Several studies have demonstrated the crucial role of pre-transplant exercise rehabilitation (prehabilitation) in patients awaiting lung transplant or major surgery in terms of postoperative muscular recovery, physical capacities, pulmonary function and quality of life without showing a significant reduction of postoperative complications or mortality [26—28]. The nutritional management of these patients plays an equally crucial role and should enable us to reduce the occurrence of complications, such as infections or surgical complications, which contribute to the risk of chronic allograft dysfunction.

Conflict of Interest

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

CRediT authorship contribution statement

Sophie Boura: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing - original draft. **François Severac:** Conceptualization, Formal analysis, Methodology, Software, Supervision, Writing - review & editing. **Omar Alali:** Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing - review & editing. **Romain Kessler:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Validation, Visualization, Writing - review & editing. **Benjamin Renaud-Picard:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing - review & editing.

Acknowledgments

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