e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 6 (2011) e142–e147

Contents lists available at ScienceDirect

e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism

journal homepage: http://www.elsevier.com/locate/clnu

Original Article

# Improvement of nutritional status in malnourished cirrhotic patients one year after liver transplantation

Manuela Merli [a,*], Michela Giusto [a], Oliviero Riggio [a], Federica Gentili [a], Antonio Molinaro [a], Adolfo Francesco Attili [a], Stefano Ginanni Corradini [a], Massimo Rossi [b]

[a] II Gastroenterologia, Policlinico Umberto I, Università Sapienza di Roma, Italy
[b] II Clinica Chirurgica, Policlinico Umberto I, Università Sapienza di Roma, Italy

ARTICLE INFO

*Article history:*
Received 29 September 2010
Accepted 5 February 2011

*Keywords:*
Malnutrition
Cirrhosis
Liver transplant
Insulin
Diet

SUMMARY

*Background & aims:* Liver transplantation is a major procedure often undertaken in patients in poor nutritional status. Few studies have examined the modification of nutritional status after liver transplantation. We aimed at analyzing the modification of nutritional status occurring in liver recipients during the first year.

*Methods:* Twenty-five consecutive patients submitted to liver transplantation were studied. A complete nutritional assessment, was performed before and at 3, 6 and 12 months after transplantation. Insulin and C-peptide plasma levels were determined and insulin sensitivity was estimated.

*Results:* According to subjective global assessment 56% of patients were malnourished at transplant. In malnourished patients nutritional status further deteriorated at 3 months but improved 6 and 12 months after transplantation. Fat mass significantly increased from before to 12 months after transplant (median triceps skinfold: 10.8 vs 15.2 mm, $p = 0.03$) while parameters of muscle mass showed minor variations (median arm muscle circumference: 23.4 vs 24.0 cm, $p = 0.3$). The daily calorie intake also improved (27 vs 32 kcal/kg/die, $p = 0.007$) and protein intake increased (0.8 vs 1.3 g/kg, $p = 0.02$). In patients without malnutrition nutritional status and dietary intake showed minor variations after transplantation. Hyperinsulinemia was normalized and insulin sensitivity improved in all patients post-transplant.

*Conclusions:* During the first 12 months after liver transplant a significant improvement in nutritional status is achieved in patients previously malnourished. Fat deposits show the more rapid improvement while the amelioration of muscle mass requires a longer period. The increased dietary intake and improved insulin sensitivity are associated to these changes.



## 1. Introduction

Orthotopic liver transplantation (LT) is a major procedure which often needs to be undertaken in patients in poor nutritional status. Malnutrition is in fact frequently associated with liver cirrhosis being its prevalence between 20 and 80% and those patients with a more advanced liver insufficiency are known to have more severe protein/calorie malnutrition.[1–4]

The pathogenesis of malnutrition in chronic liver diseases is multifactorial.[5]

Previous studies have examined the influence of nutritional status on the outcome after LT, showing that preoperative malnutrition impacts negatively on post-transplantation outcome.[6–10] In a recent prospective investigation we observed that a compromised nutritional status was independently associated with the number of infection episodes, the length of stay in the intensive care unit (ICU) and the total number of days spent in the hospital after transplantation.[11] Moreover the analysis of a large database evidenced that, among adult liver recipients, those who were transplanted being underweight had a significantly lower survival.[12] Despite the negative role of pre-transplant malnutrition and the initial disadvantage of malnourished patients, it is conceivable that these are those who, by restoring their liver function, may obtain the greater improvement. After LT, in fact, many metabolic

*Abbreviations:* LT, liver transplantation; ICU, intensive care unit; BW, body weight; MAC, mid-arm circumference; TSF, triceps skin fold; MAMC, mid-arm muscle circumference; SGA, subjective global nutritional assessment; REE, resting energy expenditure; TEI, daily total energy intake; TEE, daily total energy expenditure; TEB, total energy balance; HOMA, homeostatic model assessment index.

* Corresponding author. II Gastroenterologia, Dipartimento di Medicina Clinica, Viale dell'Università 37, 00185 Roma, Italy. Tel./fax: +39 06 49972001.
*E-mail address:* manuela.merli@uniroma1.it (M. Merli).

1751-4991/$36.00 © 2011 European Society for Clinical Nutrition and Metabolism. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.eclnm.2011.02.003

abnormalities involved in causing malnutrition are corrected, and the dietary intake may improve. The present study was aimed at analyzing the nutritional status modifications occurring during the first year after liver transplantation. Changes in anthropometric measurements, dietary intake, energy expenditure and energy balance were all recorded at time intervals and analyzed according to pre-transplant nutritional status. Modifications of the parameters of glucose metabolism during the first year after transplantation were also studied.

## 2. Patients and methods

Between June 2007 and June 2008, all consecutive patients awaiting for elective LT for end-stage liver disease at the Transplant Center of the "Sapienza" University in Rome were studied. The study was approved by the Ethical Committee of the University Hospital Policlinico Umberto I and a written informed consent was signed by all the participants.

### 2.1. General clinical and nutritional management

While awaiting for LT, all patients were followed with scheduled consultations at our Department every two/three months. Whenever needed, the patients were hospitalized for the treatment of liver disease complications. All of them received a general dietary advice based on their clinical conditions and nutritional status; a detailed dietary prescription was never adopted. The severity of cirrhosis before transplantation was classified according to the Child-Pugh[13] and the Model of End stage Liver Disease (MELD).[14] An artificial nutritional support was prescribed post-operatively only when the patient was unable to reach an adequate food intake within one week. Calcineurin inhibitors and methylprednisolone were used as primary immunosuppressants, with steroids being tapered and withdrawn after six months in the majority of patients. After hospital discharge, the subjects were seen as outpatients by an hepatologist and a surgeon with scheduled visits every 1–2 months or more frequently if needed. Each visit included the patient's examination, an evaluation of recent biochemical tests and the assessment of the possible need of therapeutic modifications. All significant clinical events after surgery (episodes of infection during hospitalization, length of stay in the ICU, length of hospitalization) and during the first year of follow up (episodes of organ rejection, surgical complications, infections, recurrence of liver disease) were recorded. The diagnosis of acute and chronic allograft rejection was based on an abnormal liver function test and on typical histological features on liver biopsy (Banff criteria). Episodes of severe acute allograft rejection were treated with 1 g metylprednisolone for three days and then gradually tapered. After transplantation, all the patients were encouraged to gradually increase their dietary intake by eating small, frequent meals and snacks. A progressive increase in their physical activity was also promoted as soon as the patient could bear it.

### 2.2. Protocol of the study

A complete nutritional assessment was performed pre-transplant and at 3, 6 and 12 month after transplantation. It included: anthropometric measurements, subjective global nutritional assessment (SGA), measurement of resting energy expenditure, estimation of calorie intake/physical activity and calculation of total energy balance. Blood samples were collected at the same time points for the determination of blood glucose, total protein, albumin, serum cholesterol, serum triglycerides, C-peptide and insulin concentrations. Patients were classified according to their nutritional status as patients without malnutrition (SGA-A) and patients with malnutrition (SGA B-C).

### 2.3. Anthropometric measurements

The anthropometric assessment was always undertaken by one observer (M.G.).

Before liver transplantation body weight (kg) was always measured after treating ascites and/or water retention with diuretics and/or paracentesis. In 3 patients with refractory ascites, dry weight was estimated also considering the amount of the remaining ascites evaluated by ultrasonography.

Mid-arm circumference (MAC, cm) was measured at the midpoint between the tip of the acromion and the olecranon process on the non-dominant side of the body by using a flexible tape measure.

Triceps skin fold (TSF) measurement (mm) was determined according to Durmin and Wormersley.[15]

All the measurements were taken on the non-dominant side of the body, with the patients standing in a relaxed position, using a Harpender skinfold caliper (John Bull British Indicators Ltd., St. Albans, UK).

Mid-arm muscle circumference (MAMC), was calculated using the MAC and the TSF according to standard equations.[16]

The subjective global nutritional assessment (SGA) was carried out according to Detsky.[17]

### 2.4. Energy metabolism

Resting Energy Expenditure (REE) was measured by indirect calorimetry with a canopy mode (Deltatrac Metabolic Monitor; Datex Instruments, Helsinki, Finland) as previously reported[11]; REE was calculated by a dedicated software.

Daily total energy intake (TEI) was evaluated through dietary interviews referring to the last seven days before the nutritional assessment. To provide a more accurate estimate of food intake, dietary interviews were carried out with the aid of a computer software [WinFood, Medimatica, Colonnella (TE), Italy] equipped with visual images of food portions. The same software was used to quantify the average daily calorie intake and the percentages of carbohydrates, lipids and proteins according to the table of food consumption of the Italian National Institute of Nutrition and the Food Composition Data Base for Epidemiologic Study in Italy[18]. The total energy intake (TEI) was expressed in kcal/day.

Each patient's physical activity was assessed by a specific questionnaire aimed at evaluating the hours spent sleeping, lying awake in bed, sitting, walking, training, etc. To calculate the energy cost of each activity, REE was multiplied by an activity factor derived from a reference Italian population.[19] Daily total energy expenditure (TEE) was obtained by the sum of the energy cost of each activity performed by each patient during the 24 h. In this calculation, the dietary-induced thermogenesis—proved to be equivalent to 10% of daily energy intake—was not considered.

The total energy balance (TEB; kcal/day) was calculated as = TEI - TEE

### 2.5. Laboratory determinations

Blood glucose, total protein, albumin, serum cholesterol and serum triglycerides were measured by standard laboratory methods. C-peptide and immunoreactive insulin were determined by radioimmunoassay. Basal insulin sensitivity was evaluated by the homeostatic model assessment index (HOMA-IR), according to the formula: fasting plasma insulin (mU/L) × fasting plasma glucose (mmol/L)/22.5.