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Obesity in Patients after Liver Transplantation

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Abstract

The aim of the present study was to evaluate the nutritional status of post-liver transplant patients. The sample consisted of a group of patients submitted to liver transplantation and a control group of patients without liver disease. Nutritional status was assessed by body composition and anthropometric methods. Body mass index indicating overweight and obesity was observed regardless of the post-liver transplantation period. Waist circumference was greater than the value recommended by the World Health Organization in the majority of post-transplant patients. Patients with a longer post-transplant period had a mean phase angle similar to that of the control group, while patients with a shorter post-transplant period had a lower mean phase angle. These results suggest a full recovery from surgery and a health improvement after transplantation since the phase angle is a measure related to nutritional status and prognosis. In conclusion, although the post-liver transplantation population studied may have had a full recovery and health improvement after surgery, obesity and excessive body fat mass are prevalent and may be deleterious in the long term in view of the associated risk of cardiovascular events.

Keywords: Liver transplantation; Obesity; Fat body mass; Phase angle

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Introduction

In recent decades, overweight and obesity have become a global public health issue. Overweight and obesity are associated with increased risks of all-cause mortality, cancer, non-alcoholic fatty liver disease, hypertension, type 2 diabetes, and metabolic syndrome [1]. The major impact of obesity on the liver is the association with non-alcoholic steatohepatitis (NASH). Indeed, NASH has emerged as one of the fastest growing indications for liver transplantation [2].

Clinical observations in long-term survivors after liver transplantation have revealed a considerable gain in body weight and an increasing prevalence of obesity [1,3]. Most of the excessive weight gain occurs in the first year of transplantation and among the causes include recovery of the appetite followed by health improvement and hyperphagia associated to the corticosteroid use and a sedentary life style [4]. At the end of the first year after liver transplantation, patients fail to replenish their total body protein, while fat mass approximates predicted values [3]. Immunosuppressive medication is often cited as a risk factor for weight gain [1].

Recently, post-transplant obesity has received interest as part of the metabolic syndrome evolving after transplantation, jeopardizing the gain in patient prognosis achieved by transplantation [2,3]. Obesity is associated with metabolic disorders and comorbidities such as coronary artery disease [2]. Moreover, cardiovascular events have been reported as a leading cause of mortality after solid organ transplantation [1].

Considering this scenario and the importance of preventing obesity in liver graft survivors, nutritional status should be monitored in all post-transplant patients, leading to appropriate nutritional treatment. The aim of the present study was to evaluate the nutritional status of post-liver transplant patients.

Method

The present study reports partial data from a major unpublished study of liver transplantation from our group conducted at Hospital das Clínicas, Ribeirao Preto Medical School, Sao Paulo University (HC-FMRP/USP) between March 2012 and December 2013. Nutritional status was assessed by body composition and anthropometric methods. The sample consisted of a group of post-liver transplantation patients (n=28) and a control group of patients without liver disease (n=23).

Table 1: Anthropometric assessment of post-transplant patients.

	Post-transplant group (n=28)		Control group (n=23)	ANOVA	
	< 1 y (n=9)	≥ 1 y (n=19)		95% CI	*p value*
Weight (kg)	72.69 ± 9.3	79.18 ± 12.0	79.45 ± 16.6	-7.48;20.47[a] -10.97;10.44[b] -20.34;6.82[c]	0.4358
BMI (kg/m²)	25.73 ± 1.9	28.49 ± 4.8	29.09 ± 6.7	-2.69;8.21[a] -4.78;3.58[b] -8.66;1.94[c]	0.2935
AC (cm)	29.94 ± 2.4	32.97 ± 4.4	33.41 ± 3.9	-0.87;6.93[a] -3.43;2.55[b] -7.26;0.32[c]	0.0783
MAC (cm)	22.70 ± 2.21	25.43 ± 3.24	25.73 ± 2.55	-0.061;5.52[a] -2.437;1.84[b] -5.742;-0.314[c]	0.0233
AFA (cm²)	20.62 ± 4.693	24.71 ± 9.387	24.70 ± 7.891	-4.026;12.19[a] -6.209;6.216[b] -11.96;3.800[c]	0.3954
MAA (cm²)	31.87 ± 7.516	43.08 ± 12.56	43.89 ± 10.44	0.2879;22.15[a] -9.181;7.566[b] -22.65;-1.406[c]	0.0195
AbC (cm)	97.43 ± 7.366	102.3 ± 10.33	101.0 ± 13.69	-6.804;16.52[a] -7.631;10.24[b] -14.88;7.776[c]	0.5881
BST (mm)	9.778 ± 4.008	12.76 ± 8.496	14.24 ± 8.814	-5.129;11.10[a] -7.697;4.737[b] -12.35;3.419[c]	0.3784
TST (mm)	23.02 ± 7.655	24.06 ± 9.298	24.47 ± 11.29	-11.11;9.031[a] -11.24;8.334[b] -8.127;7.305[c]	0.9346
SST (mm)	15.54 ± 3.346	24.15 ± 10.54	27.38 ± 13.03	-2.455;19.66[a] -11.71;5.236[b] -22.58;-1.094[c]	0.0310
IST (mm)	15.54 ± 3.346	24.15 ± 10.54	27.38 ± 13.03	-3.359;18.66[a] -10.03;6.167[b] -20.31;1.139[c]	0.0949

Data are reported as mean and standard deviation. [a]comparing ≥1 year post-transplant and <1 year post-transplant. [b]comparing ≥ 1 year post-transplant and control group.[c]comparing <1 year post-transplant and control group.
BMI: Body Mass Index; AC: Arm Circumference; MAC: Muscle Arm Circumference; AFA: Arm Fat Area; MAA: Muscle Arm Area; AbC: Abdominal Circumference; BST: Biceps skinfold thickness; TST: Triceps Skinfold Thickness. SST: Subscapular Skinfold Thickness; IST: Iliac Skinfold Thickness.

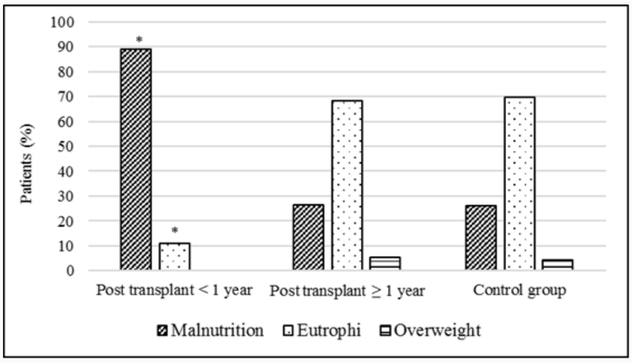

Figure 1: Nutritional status of the post-transplant and control groups according to muscle arm circumference. *p=0.002 for malnutrition between groups and p=0.0059 for normal weight between groups.

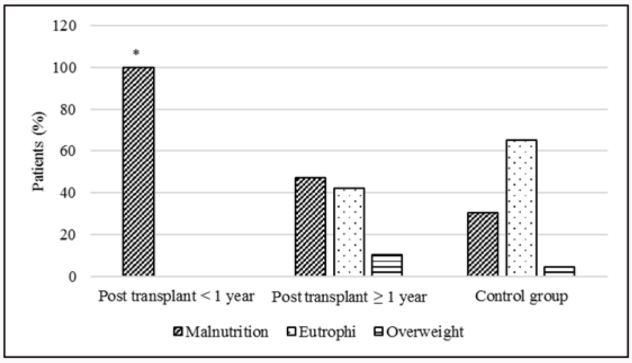

Figure 2: Nutritional status of the post-transplant and control groups according to muscle arm area. *p=0.0019 for malnutrition between groups.

The post-transplant group consisted of patients aged ≥18 years with a post-liver transplantation period >30 days. Exclusion criteria were chronic kidney disease, acute or chronic respiratory failure, infectious pulmonary disease, untreated hyperthyroidism or hypothyroidism, and locomotor disability. Patients with diagnosis of graft rejection were excluded from the sample. The post-transplant group was divided into two subgroups according to post-transplant period, i.e., <1 year and ≥1 year.

The control group consisted of outpatients aged ≥18 years seen at the Urology Clinic of HCFMRP-USP, matched to the post-transplant patients for gender, age and body mass index (BMI). Eligibility criteria included absence of alcohol consumption and of acute or chronic liver disease, renal failure, pulmonary disease, cancer, hyperthyroidism, hypothyroidism, and locomotor disability. Biochemical analyses of albumin, aminotransferases, total protein, cholinesterase, lactate dehydrogenase, bilirubin, alkaline phosphatase and glutamyl transferase were carried out according to standard methodologies [5-12] at the Laboratory of the Surgery Department, HCFMRP-USP, in order to determine liver function.

Anthropometric measurements of weight, height, arm and abdominal circumferences and skinfold thickness were performed

Table 2: Tetrapolar bioelectrical impedance of patients.

	Post-transplant group (n=28)		Control group (n=23)	ANOVA	
	<1 y (n=9)	≥ 1 y (n=19)		95% CI	*p* value
Total fat-free mass (kg)	54.47 ± 9.439	53.55 ± 7.659	54.11 ± 8.443	-9.29;7.45[a] -6.97;5.85[b] -7.78;8.49[c]	0,9574
Total fat mass (kg)	18.46 ± 3.014	25.62 ± 7,828	25.34 ± 10.46	-1.51;15.84[a] -6.37;6.93[b] -15.31;1.55[c]	0.0974
Total body water (L)	39.43 ± 6.833	38.30 ± 5.552	38.91 ± 6.401	-7.33;5.07[a] -5.36;4.14[b] -5.50;6.55[c]	0,8936
Phase angle (º)	5.656 ± 1.017	6.689 ± 0.8563	6.722 ± 0.7810	0.178;1.89[a] -0.69;0.62[b] -1.898;-0.24[c]	0.0063
Reactance (Ω)	50.68 ± 12.44	64.41 ± 9.837	61.93 ± 9.507	3.52;23.95[a] -5.35;10.30[b] -21.18;-1.33[c]	0.0056
Resistance (Ω)	509.3 ± 72.54	552.0 ± 71.94	527.7 ± 68.08	-27.87;113.3[a] -29.83;78.30[b] -87.03;50.11[c]	0.2907

Data are reported as mean and standard deviation. [a]comparing ≥1 year post-transplant and <1 year post-transplant. [b]comparing ≥1 year post-transplant and control group.[c]comparing <1 year post-transplant and control group.

Table 3: Segmental bioelectrical impedance of the patients.

	Body Segment	Post-transplant group (n=28)		Control group (n=22)	ANOVA
		< 1 y (n=9)	≥ 1 y (n=19)		*p* value
Fat-free mass (kg)	Left upper limb	2.79 ± 0.61	2.78 ± 0.56	2.92 ± 0.61	0.7064
	Right upper limb	2.84 ± 0.60	2.82 ± 0.58	2.86 ± 0.61	0.9795
	Trunk	28.87 ± 4.76	27.80 ± 4.16	28.40 ± 4.19	0.8105
	Left lower limb	9.11 ± 1.56	8.82 ± 1.38	8.69 ± 1.58	0.7837
	Right lower limb	9.31 ± 1.75	8.92 ± 1.37	8.76 ± 1.60	0.6668
Fat mass (kg)	Left upper limb	0.86 ± 0.14	1.31 ± 0.67	1.32 ± 1.04	0.3188
	Right upper limb	0.83 ± 0.16	1.19 ± 0.60	1.22 ± 0.89	0.3529
	Trunk	10.43 ± 2.80	14.36 ± 4.25	13.07 ± 4.99	0.0992
	Left lower limb	2.17 ± 0.67	3.58 ± 1.82	3.94 ± 2.44	0.0900
	Right lower limb	2.14 ± 0.70	3.61 ± 1.90	4.11 ± 2.56	0.0712

Data are reported as mean and standard deviation

for nutritional assessment. Measurements were made according to standard methods using calibrated equipment. BMI was classified according to standard references for adults [13] and elderly subjects [14]. Arm muscle circumference, arm muscle area and arm fat area were assessed by equations and considered to represent malnutrition, normal weight and obesity according to reference values for gender and age [15-18].

Body composition was assessed by 50 kHz single frequency electric bioimpedance using a Biodynamic Analyzer 310 model (*Biodynamics Corporation*, Seattle, WA, USA) for the tetrapolar method and using an Ironman Segmental Compositor BC-558 (*Tanita Corporation*, Toquio, Japan) for the segmental method, according to standard methods and with the patient fasted for at least 4 h.

Food consumption was assessed by a trained dietitian using a habitual food record.

Statistical analyses were performed using the Prism GraphPad 4.0 software (San diego, CA, USA). Data are reported as mean and standard deviation for continuous quantitative variables. The Student *t* test and ANOVA (with Bonferroni's post-test) were used to compare two or more independent groups. The chi-square test was applied to categorical variables. The level of significance was set at 5% in all tests.

The study was approved by the Ethics Committee o HCFMRP-USP and all subjects gave written informed consent to participate.

Results

Sample consisted of 5 women and 23 men. Main causes of liver transplantation were by alcoholic cirrhosis (29%), followed by cryptogenic cirrhosis (21%), alcoholic cirrhosis associated to virus C hepatitis (14%), virus C hepatitis cirrhosis (14%) and other causes as virus B hepatitis (n=1), virus B associated to virus D hepatitis (n=1), autoimmune hepatitis cirrhosis (n=1), familiar paramyloidosis (n=1), alfa-1 antitrypsin deficiency (n=1), and primary biliary cirrhosis (n=1). Immunosuppressive medication consisted most of tacrolimus (50%), followed by tacrolimus associated to mofetil micofenolate (43%), mofetil micofenolate (4%) and sirulimus (4%).

Antropometric data are shown in Table 1. Mean muscle arm circumference and mean muscle arm area differed statistically between groups. A higher frequency of muscle mass deficit (Figures 1 and 2) was observed in the <1 year post-transplant group regarding muscle arm circumference and muscle arm area. Sub-scapular skinfold thickness differed significantly between groups.

Tetrapolar bioelectrical impedance data are presented in Table 2 and segmental bioelectrical impedance data are presented in Table 3. There was no significant difference in body fat mass or body fat-free mass between groups according to both the tetrapolar and segmental methods. Phase angle was significantly lower in the <1 year post-transplant group. Energy and macronutrient intake did not differ significantly between groups.

Waist circumference was greater than the value recommended by the WHO [19], of 94 cm for men and 80 cm for women, in 78% of <1 year post-transplant patients and in 79% of ≥1 year post-transplant patients.

Discussion

The present study contributed important results to the literature by corroborating with recent findings about the nutritional status of liver transplant recipients.

Body mass index values indicating overweight and obesity were observed in liver transplant patients regardless of post-liver transplantation period. Waist circumference demonstrated higher severe risks of cardiovascular events in the majority of patients. Excessive weight gain (more than 10 kg) during the first year after liver transplantation has been reported [1], with a 40% incidence of obesity in this population in the first post-transplant year [20] and an incidence of about 70% three years after transplantation [21,22].

Studies have described an increased prevalence of dyslipidemia, hypertension and diabetes mellitus in liver transplant recipients. Together with the excessive body weight, these conditions contribute to the occurrence of metabolic syndrome and the increasing risk of cardiovascular events, which are the main cause of death after transplantation [23,24].

Although the difference was not significant, fat body mass was greater in patients with ≥1 year of liver transplantation, while lean body mass was similar for the two groups. It is possible that the recovery of body mass does not occur proportionally between fat and lean mass in post-liver transplanted patients.

Increased food intake, physical inactivity and immunosuppressive therapy have been described as possible causes of obesity in liver transplant patients [7].

Phase angle, a measure of bioimpedance analysis, was similar between patients with a longer post-transplant period and controls, while patients with a shorter post-transplant period had a lower mean phase angle. These results suggest a full recovery from surgery and improved health after transplantation since phase angle is a measure associated with nutritional status and prognosis [25].

In conclusion, although the post-liver transplantation population studied here may have had a full recovery and health improvement after surgery, obesity and excessive fat body mass are prevalent and may be deleterious in the long term considering the associated risk of cardiovascular events.

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The author's responsibilities were as follows –Silva MA: accountable for research execution and manuscript preparation. Jordão AA: accountable for research supervision and revision of the manuscript. Castro e Silva O: mentor of the research, accountable for research supervision and revision of the manuscript.

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