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Nutritional status, lipid profile and HOMA-IR in post-liver transplant patients

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Abstract

Introduction: **A high prevalence of overweight, obesity, diabetes and dyslipidemia has been reported following liver transplantation (LT). Although these conditions are known to induce an increased risk for cardiovascular events, which are among the major causes of death in post-LT patients, much debate remains in the literature regarding the applicability of different nutritional assessments methods to this population.**

Objective: **To assess the nutritional status, lipid profile, homeostatic model assessment of insulin resistance (HOMA-IR) and dietary intake adequacy in the post-LT period.**

Methods: **Cross-sectional study of patients after a maximum of 2 years post-LT, involving the assessment of body mass index (BMI), percent weight loss, arm (AC) and arm muscle circumference (AMC), triceps skinfold (TSF), neck (NC) and waist (WC) circumference, lipid profile, HOMA-IR and percent adequacy of dietary intake.**

Results: **In the group of 36 patients, 61.1% were male, mean age 53.2 years (± 10.6). Severe weight loss was noted in 66.7% of patients. Most individuals were eutrophic according to BMI, AC and AMC, while TSF showed malnutrition, NC demonstrated overweight and WC showed metabolic risk. Dyslipidemia was diagnosed in 87.5% of patients, and insulin resistance in 57% of the patients. Most patients had adequate dietary intake, although the time since transplant was positively correlated with AC (r = 0.353; p = 0.035) and negatively correlated with vitamin A intake (r = - 0.382; p = 0.022), with the caloric adequacy (r = -0.338; p = 0.044) and vitamin A adequacy (r = -0.382; p = 0.021).**

Conclusion: **Although anthropometry provided somewhat variable nutritional diagnoses, when combined with biochemical tests, findings showed the prevalence of cardiovascular risk. As such, patients should be provided with transdisciplinary assistance, and strategies should be developed so as to reduce the risk factors recorded in this population.**

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Key words: *Liver transplantation. Nutritional status. Dyslipemia.*

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ESTADO NUTRICIONAL, PERFIL LIPÍDICO Y HOMA-IR EN EL POSTRANSPLANTE HEPÁTICO

Resumen

Introducción: **En el postransplante hepático (TH) hay un aumento de prevalencia de sobrepeso, obesidad, diabetes y dislipidemia. Esos factores están asociados al riesgo de enfermedades cardiovasculares, una de las principales causas de mortalidad en el post-TH. Sin embargo, no se han establecidos cuáles son los mejores métodos de evaluación nutricional de esta población.**

Objetivo: **Evaluar el estado nutricional, perfil lipídico, homeostatic model assessment of insulin resistance (HOMA-IR) y adecuación de ingestión dietética en el post-TH.**

Métodos: **Estudio transversal, incluidos pacientes hasta con 2 años de TH evaluándose por el índice de masa corporal (IMC), porcentaje de pérdida de peso, circunferencia del brazo (CB) y muscular del brazo (CMB), pliegue tricipital (PT), circunferencia del cuello (CP) y de la cintura (CC), perfil lipídico, HOMA-IR y porcentaje de adecuación de ingestión dietética.**

Resultados: **De los 36 pacientes, 61,1% eran de sexo masculino, con un promedio de edad de 53,2 años (± 10,6). En 66,7% de los evaluados, hubo pérdida severa de peso. Hubo predominio de eutrofia por el IMC, CB y CMB, desnutrición por el PT, sobrepeso por la CP y CC muy alta. Se constató dislipidemia en el 87,5% de los pacientes y resistencia a la insulina en el 57%. La mayoría presentó adecuación de la ingestión dietética, pero el tiempo de TH se correlacionó positivamente a la CB (r = 0,353; p = 0,035) y negativamente a la ingestión de vitamina A (r = -0,382; p = 0,022), adecuación calórica (r = -0,338; p = 0,044) y de vitamina A (r = -0,382; p = 0,021).**

Conclusión: **Aunque la antropometría indicó variabilidad en el diagnóstico nutricional, cuando se combina con la evaluación bioquímica, los resultados mostraron la prevalencia de riesgo cardiovascular. Los pacientes deben recibir acompañamiento transdisciplinario, y se deben desarrollar estrategias para reducir los factores de riesgo de la población.**

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Palabras clave: *Trasplante hepático. Estado nutricional. Dislipidemia.*

Abbreviations

AC: Arm circumference.
AMC: Arm muscle circumference.
BMI: Body mass index.
DM: Diabetes mellitus.
EAR: Estimated average requirements for groups.
HDL:High-density lipoprotein.
HOMA-IR: Homeostatic model assessment of insulin resistance.
LDL: Low-density lipoprotein.
LT: Liver transplantation.
MELD-Na: MELD-sodium.
NC: Neck circumference.
TSF: Tricipital skinfold thickness.
WC: Waist circumference.

Introduction

Metabolic complications have been increasingly reported following liver transplantation (LT).[1] LT is the preferred treatment for patients with uncompensated cirrhosis, hepatocarcinoma and acute hepatic insufficiency.[2] Malnutrition is a common finding among patients scheduled for LT, as it is a frequent consequence of cirrhosis, and has been shown to be associated with higher morbidity and mortality rates in these individuals. Some studies also suggest that malnutrition may persist following LT.[3] On the other hand, recent years have also seen an increase in the prevalence of overweight and obesity in post-LT patients, which is often mistakenly interpreted to be a sign of nutritional recovery.[4,5]

Although survival rates among LT patients have increased[6], studies have also found the occurrence of insulin resistance[7] and an increase in the prevalence of dyslipidemia, hypertension, and diabetes mellitus (DM) among these individuals. Together with excess weight, these conditions contribute to the occurrence of metabolic syndrome and to the risk of cardiovascular diseases,[8] which is one of the main causes of death following LT[2].

Although there are a number of ways to assess patients' nutritional status, several methodological difficulties have been found with regard to these processes.[9] Furthermore, despite the high frequency of metabolic complications observed in adult LT recipients, few studies have involved the nutritional assessment of these patients.[10] Therefore, the aim of the present study was to investigate the nutritional status of post-LT patients through anthropometric assessment, lipid profile, homeostatic model assessment of insulin resistance (HOMA-IR) and dietary adequacy.

Methods

Sample

A cross-sectional study was conducted using the following inclusion criteria: age equal to or greater than 19 years, having undergone a LT within 1 to 24 months prior to study enrollment, being in adequate conditions for assessment, and agreeing to participate by providing written informed consent. Retransplant patients, pregnant women, and individuals with physical conditions which interfered with anthropometric measurements were excluded from the study. The sample was divided according to time since each patient's LT (Il- 12 months and 12I- 24 months). Data were collected at the Gastroenterology Outpatient Clinic of the Hospital de Clinicas de Porto Alegre between November 2012 and March 2013. The present study was approved by the research ethics committee of the institution in which it was conducted (protocol number 120373) and all patients signed a written informed consent form.

The following demographic and clinical variables were collected from patient records: sex, age, time since LT, etiology of liver disease and reason for LT (as confirmed by biochemical, clinical and anatomopathological tests), MELD-sodium score (MELD-Na), time on the waiting list, duration of hospitalization, medication use and comorbidities.

Anthropometric assessment

All anthropometric assessments were conducted by the same examiner, and involved the measurement of the following variables: weight, height, body mass index (BMI), percentage of weight loss, arm circumference (AC), triceps skinfold thickness (TSF), arm muscle circumference (AMC), waist circumference (WC) and neck circumference (NC). Weight was measured using a digital scale (Filizola®, São Paulo, Brazil). While being weighed, all patients wore light clothing, were barefoot, and had no objects in their pockets. When edema was present, weight was corrected for the estimated weight of the edema fluid (ankle edema: 1 kg).[11] Height was assessed using a vertical stadiometer (Balmak®, São Paulo, Brazil). During height measurements, patients were barefoot, wore no accessories on their heads, and had their heads positioned in the Frankfurt plane. Patients were classified into adult (malnutrition: < 18.49 kg/m^2; eutrophy 18.5 to 24.9 kg/m^2; overweight: 25 to 29.9 kg/m^2; obesity: > 30 kg/m^2)[12] or elderly (malnutrition: < 22 kg/m^2; eutrophy: 22 to 27 kg/m^2; overweight: > 27 kg/m^2)[13] BMI categories, as applicable. The percentage of weight loss was calculated based on each patient's usual weight, and classified according to the Blackburn model (significant weight loss: 1 to 2% in 1 week, 5% in 1 month, 7.5% in 3 months or 10% in 6 months; severe weight loss: > 2% in 1 week, > 5% in 1 month, > 7.5% in 3 months or > 10% in 6 months)[14].

Circumferences were measured using a non-stretchable measuring tape (Sanny®, São Paulo, Brazil), with the patient in a standing position, and in triplicate (so as to reduce intraobserver variability). WC was measured and classified according to World Health Organization criteria (increased risk of metabolic complications: > 94 cm in men and > 80 cm in women; greatly increased risk of metabolic complications: > 102 cm in men and > 88 cm in women).[15] NC was measured with the patient standing face to face with the examiner, and the measuring tape placed between mid-cervical spine and mid-anterior neck. In men with a laryngeal prominence, the NC was measured by placing the tape just below this point. NC measurements were classified according to the system proposed by Ben-Noun, Sohar and Laor (overweight: > 37 cm in men and > 34 cm in women; obese: > 39.5 cm in men and > 36.5 cm in women).[16]

The TSF was measured in triplicate using a Lange Skinfold Caliper *(Beta Technology Incorporated* Cambridge, Maryland, USA) with a constant pressure of 10 g/mm^2. The adequacy percentage of AC and TSF measurements (% adequacy = measurement obtained ÷ 50th percentile measurement x 100) was calculated and classified (malnutrition: < 90%; eutrophy: ≥ 90 and < 110%; overweight: ≥ 110 and ≥ 120%; obesity: ≥ 120%), as were AMC values (malnutrition: ≥ 90%; eutrophy: > 90%).[17]

Dietary Intake Assessment

A 24-hour dietary recall was conducted on the same day the anthropometric assessments were conducted, and a photographic record of the portions of food consumed by patients was used so as to improve the quality of the data collected. Dietary intake was calculated using the Nutwin®-Nutrition Support Software (Universidade Federal de São Paulo, São Paulo, Brazil), version 1.6, 2010. The type and amount of dietary supplements consumed was also assessed.

Energy requirements were calculated using the Harris and Benedict equation (for men: 66.5 + 13.8 x weight in kg + 5 x stature in centimeter - 6.8 x age in years; for women: 655 + 9.6 x weight in kg + 1.8 x stature in centimeter - 4.7 x age in years),[18] using activity (1.25 for bedridden patients and 1.3 for active ones) and injury (1 for patients without complications) factors to assess total energy expenditure. Intake recommendations were used to assess protein,[19] cholesterol, and dietary fiber intake;[20] the recommended intake for iron, zinc, and vitamins A and C was drawn from Estimated Average Requirements for Groups (EAR), and calcium was assessed according to Adequate Intake, since EAR for calcium were unavailable.[21] The percent adequacy was calculated for each of these nutrients (% adequacy = amount ingested ÷ amount recommended x 100).

Biochemical assessment

Blood samples were drawn after a 12 h fast, and used to assess serum concentrations of total cholesterol, triglycerides and high-density lipoprotein (HDL) cholesterol through colorimetry (Advia 1800, Siemens®, NY, USA), and of low-density lipoprotein (LDL) through the Friedewald equation.[22] Results were then classified according to the recommended.[20] Insulin levels were determined by chemiluminescence (Advia Centaur XP, Siemens®, NY, USA), and glucose levels were measured using an enzyme hexokinase method (Advia 1800, Siemens®, NY, USA). The coefficients of variation for cholesterol, triglycerides, HDL, glucose and insulin were 3.35%, 2.69%, 5.03%, 3.45% and 7.55%, respectively. The HOMA-IR was classified using a cut-off value of 2.71 for insulin resistance.[23]

Statistical analysis

Quantitative variables were descriptively analyzed using means and standard deviations or medians and interquartile ranges, while categorical variables were expressed as frequencies and percentages. Person and Spearman correlation coefficients (for parametric and nonparametric variables, respectively) were used to assess the correlation between time since the LT and anthropometric, biochemical and dietary variables. The kappa test was used to assess the concordance between BMI < 25 kg/m^2 and AC, TSF and AMC values, as well as between BMI > 25 kg/m^2 and AC, TSF and NC measurements. Results were considered significant at $p < 0.05$. Data were analyzed using the Statistical Package for Social Sciences software, version 19.0.

Results

A total of 37 patients met inclusion criteria during the study period. However, one patient refused to participate, so that only 36 patients were included in the final sample. All individuals underwent orthotopic LT.

Table I contains the demographic and clinical characteristics of the study sample.

Table II contains patients' nutritional status as determined by anthropometry. The TSF measurements of four patients (11%) and the AC and AMC of two patients (5.60%) indicated severe malnutrition. WC measurements could not be obtained from the five patients (13.90%) who had incisional hernia. Weight loss was detected in 12 patients (33.30%).

A positive Pearson's correlation was found between the percent adequacy AC and time since LT ($r = 0.353$; $p = 0.035$). There were no significant correlations among the remaining anthropometric variables, and no concordance between BMI classifications and those of the other anthropometric indicators assessed.

Twenty-eight patients (87.50%) were diagnosed with dyslipidemia according to biochemical assessment. Table III contains patients' nutritional status according to the results of these tests. Six (50%) of the

Table I
Demographic and clinical characteristics of post-liver transplant patients

Characteristics	*Results*
Sex	
Male	22 (61.10)
Age (years)	53.25 ± 10.62
Time on the waiting list (days)	187 (114.25-282.25)
Time since LT (months)	10.50 (3.50-16.75)
1|-12	19 (52.78)
12|-24	17 (47.22)
Etiology of liver disease	
HCV	12 (33.30)
Alcohol	2 (5.60)
HCV+Alcohol	4 (11)
HBV	1 (2.80)
HBV+Alcohol	1 (2.80)
NAFLD	2 (5.60)
Hemochromatosis + HCV	5 (13.90)
Hemochromatosis + HCV + Alcohol	1 (2.80)
Biliary cirrhosis	3 (8.30)
Other	5 (13.90)
Reason for transplant	
Uncompensated cirrhosis	11 (30.60)
HCC	25 (69.40)
MELD-Na	23 ± 10.15
Duration of hospitalization (days)	17 (13-25.50)
Comorbidities	
DM2	19 (52.80)
Hypertension	14 (38.90)
DM2 and hypertension	9 (25)
Immunosuppresants	
Cyclosporine	1 (2.80)
Tacrolimus	33 (91.70)
Prednisone	23 (63.90)
Mycophenolate mofetil	36 (100)
Sirolimus	3 (8.30)

LT: Liver transplant. HCV: Hepatitis C virus. HBV: Hepatitis B virus. NAFLD: Non-alcoholic fatty liver disease. HCC: hepatocellular carcinoma. DM2: Type 2 diabetes mellitus. MELD-Na: MELD-sodium score.
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

12 patients without DM who underwent biochemical tests were found to be insulin resistant. Of the 16 patients with type II DM whose test results were available, six (37.50%) were not diagnosed as insulin resistant. No correlations were found among biochemical test results and time since LT.

Analyses of nutritional supplement use revealed that ten (27.80%) patients took calcium carbonate supplements, nine (25%) took vitamin D and one (2.80%) made use of vitamin A supplements. Only two of these patients (5.60%) had calcium adequacy. The patient who took vitamin A supplements did not have adequacy. Data regarding dietary intake and adequacy are displayed in table IV.

Spearman correlation coefficients revealed negative correlations between the time since LT and the caloric adequacy ($r = -0.338$; $p = 0.044$) and vitamin A intake ($r = -0.382$; $p = 0.022$), and the adequacy of vitamin A ($r = -0.382$; $p = 0.021$). No correlations were observed among the time since LT and the remaining dietary variables.

Discussion

The present study characterized the nutritional profile of patients up to 2 years post-LT. The sample demonstrated the prevalence of the following: 1) malnutrition, according to TSF, 2) eutrophy according to BMI, AC and AMC, 3) overweight according to NC, 4) risk of metabolic complications as indicated by WC and 5) dyslipidemia and insulin resistance. The time since LT was also found to be positively correlated with AC, and negatively correlated with vitamin A intake, and with calorie and Vitamin A adequacy. These data illustrate the nutritional alterations as well as the cardiovascular risk of patients in the post-LT period.

The present study confirms the findings of other studies in the literature regarding the predominance of male patients and the prevalence of hepatitis C and of hepatocellular carcinoma among LT patients.[24] In the present study, mean MELD-Na scores were found to be higher than those obtained by the other analyses conducted, and MELD-Na values have also been found to be superior to MELD values in predicting the survival of patients with more severe conditions.[25] Therefore, MELD-Na scores were selected for use in the present study. The high prevalence of type 2 DM and hypertension found in the present study may be explained by the fact that these conditions are frequently reported after LT.[26] However, the present study did not investigate whether the patients who presented with these conditions were diagnosed before or after their transplants.

A high prevalence of eutrophy was also identified based on the following anthropometric parameters: AC (a measure of muscle and adipose tissue), AMC (a measure of muscle tissue), and BMI, which does not distinguish between these two types of tissue. The present findings regarding the prevalence of eutrophy were similar to those obtained in a previous cross-sectional study of patients who were, on average, 4 years post-LT.[9] Although a lower frequency of eutrophy has been observed in LT patients in other studies in the literature, these investigations were conducted on patients who were at least 2 years post-LT, and used lower cutoff scores for eutrophy.[4] The high prevalence of obesity demonstrated by TSF in the present study is in agreement with a previous study on cirrhotic patients, which found that TSF values may increase significantly in the first year post- LT. Such findings underscore the importance of using multiple anthropometric methods since, at the time of writing, there is no gold standard for this type of evaluation,[27] and the combination of several assessment methods, like bioelectrical impedance, could be used to yield more reliable results.

Table II
Anthropometric assessment of post-liver transplant patients

Anthropometric variables	*Time since LT (months)* 1|-12 (n = 19)	12|-24 (n = 17)	*Total (n = 36)*
Weight (kg)	70.95 ± 15.26	74.18 ± 15.76	72.47 ± 15.36
BMI (kg/m²)	24.63 ± 5.14	26 ± 5.86	25.58 ± 5.56
Malnutrition	1 (56.26)	2 (11.76)	3 (8.30)
Eutrophy	9 (47.37)	6 (35.30)	15 (41.70)
Overweight	7 (36.84)	6 (35.50)	13 (36.10)
Obesity	2 (10.53)	3 (17.65)	5 (13.90)
% Weight Loss*	11 (6-21)	9 (2-9)	9 (4.5-13.25)
Significant	–	1 (20)	1 (8.30)
Severe	6 (85.71)	2 (40)	8 (66.70)
Non-significant	1 (14.29)	2 (40)	3 (25)
% AC adequacy	93.42 ± 17.28	100.59 ± 16.14	96.80 ± 16.90
Malnutrition	8 (42.11)	4 (23.53)	12 (33.30)
Eutrophy	4 (21.05)	7 (41.18)	14 (38.90)
Overweight	7 (36.84)	4 (23.53)	8 (22.20)
Obesity	–	2 (11.76)	2 (5.60)
% TSF adequacy	96.37 ± 42.29	109.94 ± 38.61	102.78 ± 40.60
Malnutrition	10 (52.63)	4 (23.53)	14 (38.90)
Eutrophy	3 (15.79)	5 (29.41)	8 (22.20)
Overweight	2 (10.53)	3 (17.65)	5 (13.90)
Obesity	4 (21.05)	5 (29.41)	9 (25)
% AMC adequacy	95.21 ± 17.44	100.82 ± 16.60	97.86 ± 17.05
Malnutrition	7 (36.84)	4 (23.53)	11 (30.60)
Eutrophy	12 (63.16)	13 (76.47)	25 (69.40)
WC (cm) †	94.29 ± 12.88	95.93 ± 15	95.03 ± 13.66
Adequate	6 (35.30)	4 (28.57)	10 (32.30)
Increased	5 (29.40)	4 (28.57)	9 (29)
Very high	6 (35.50)	6 (42.86)	12 (38.70)
NC (cm)	26.05 ± 3.82	36.12 ± 3.08	36.08 ± 3.44
Eutrophy	7 (36.84)	8 (47.06)	15 (41.70)
Overweight	9 (47.37)	7 (41.18)	16 (44.40)
Obesity	3 (15.79)	2 (11.76)	5 (13.90)

LT: Liver transplant.BMI: Body mass index. AC: arm circumference. TSF: triceps skinfold. AMC: arma muscle circumference. WC: waist circumference. NC: neck circumference.
*Data corresponding to 12 participants (1|-12 = 7; 12|-24 = 5). †Data corresponding to 31 participants (1|-12 = 17, 12|-24 = 14).
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

WC measurements suggested that a significant proportion of patients had a greatly increased risk of metabolic complications due to excess visceral fat. These results are similar to those obtained by other studies in the literature, although these investigations used different assessment methods.[24,28] Given the high incidence of incisional hernia following LT, especially in women and in patients with a BMI over[29] 25 kg/m², some post-LT patients are unable to undergo WC measurements. However, NC results did indicate a high prevalence of overweight and provided a measure of upper body fat distribution. Given the limitations of WC measurements, the assessment of NC may be a more adequate method of assessing body fat distribution in this population. An extensive literature search revealed no studies of post-LT patients involving NC measurements. These results underscore the high prevalence of overweight and risk of metabolic complications following LT.

A number of patients in the present study were also found to be malnourished, especially according to TSF, which provide an assessment of adipose tissue. Similar to the present study, some investigations have found poor TSF adequacy in early and late post-LT patients; however, unlike the present investigation, these studies have also reported a low AMC adequacy in these individuals[30]. The prevalence of severe weight loss was also found to be high, especially in recently transplanted patients, which may reflect the resolution of the edema and ascites developed as a consequence of hepatic disease.[10] Interestingly, BMI indicated a low prevalence of malnutrition, confirming that this method should be used in combination with other assessments[31] so as to provide a better evaluation of nutritional status after LT.

The present results indicated that both malnutrition and overweight may occur during the first two years post-LT. The anthropometric methods used allowed

Table III
Biochemical assessment of post-liver transplant patients

Biochemical tests	*Time since LT (months)* 1|-12 (n = 19)	12|-24 (n = 17)	Total (n = 36)
Cholesterol (mg/dL)*	167.06 ± 50.20	155.60 ± 30.01	161.85 ± 42.03
Adequate	13 (72.22)	13 (86.67)	26 (78.80)
High	5 (27.78)	2 (13.33)	7 (21.20)
LDL (mg/dL)†	95.59 ± 36.89	90.47 ± 25.68	93.19 ± 31.73
Adequate	16 (94.112)	15 (100)	31 (96.90)
High	1 (5.88)	–	1 (3.10)
HDL (mg/dL)†	43.53 ± 19.65	38.67 ± 8.38	41.25 ± 15.40
Adequate	5 (29.41)	4 (26.67)	9 (28.10)
Low	12 (70.59)	11 (73.33)	23 (71.90)
Triglycerides (mg/dL)†	172.76 ± 78.36	130.33 ± 48.81	152.88 ± 68.61
Adequate	8 (47.06)	10 (66.67)	18 (56.30)
High	9 (52.94)	5 (33.33)	14 (43.80)
HOMA-IR‡	250 (1.25-5)	2.50 (1-7)	2.50 (1-5)
Resistance	10 (62.50)	6 (50)	16 (57.10)
No resistance	6 (37.50)	6 (50)	12 (42.90)

LT: Liver transplant. LDL: low-density lipoprotein. HDL:High-density lipoprotein. HOMA-IR: Homeostatic model assessment of insulin resistance.
*Data corresponding to 33 participants (1|-12 = 18; 12|-24 = 15). †Data corresponding to 32 participants (1|-12 = 17, 12|-24 = 15). ‡Data corresponding to 28 patients (1|-12 months = 16; 12|-24 = 12).
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

Table IV
Dietary intake and adequacy of post-liver transplant patients

Nutrients	*Time of LT (months)* 1|-12 (n = 19)	12|-24 (n = 17)	Total (n = 36)
Energy (kcal)	1601 (1419-2283)	1606 (1341-2172)	1603.50 (1424.50-2174)
% Adeq.	95 (71-110)	85 (66-100.50)	85.50 (67.25-107.75)
Carbohydrates (g)	226 (178-301)	242 (177-266.50)	228.50 (180.50-284)
Lipids (g)	53 (40-64)	52 (39.50-65.50)	52.50 (40-64.75)
Protein (g/kg of CW)	0.99 (0.78-1.49)	1.04 (0.67-1.43)	1 (0.70-1.43)
% Adeq.	99 (78-149)	104 (67.50-143)	100 (70.25-143.50)
Calcium mg	788 (644-1371)	713 (421-901.50)	748.50 (502.75-992.25)
% Adeq.	78 (53-114)	62 (45-79.50)	67 (51-84)
Iron (mg)	10 (8-15)	11 (9.50-14)	10.50 (8.25-14)
% Adeq.	175 (149-254)	211 (166.50-242)	201 (155.75-249.75)
Zinc (mg)	9 (7-11)	10 (6-13.50)	9 (7-11.75)
% Adeq.	110 (90-148)	123 (87-161.50)	119 (90.75-154)
Vit. A (RE)	658 (243-1920)	351 (215.50-706.50)	466.50 (240-1097)
% Adeq.	105 (39-260)	58 (34-113.50)	87 (38.25-140.50)
Vit. C (mg)	121 (28-177)	74 (20-194.50)	91 (27.25-175)
% Adeq.	175 (37-263)	115 (29.50-287)	126 (36.25-276.50)
Dietary fiber (g)	15 (10-32)	18 (12-29)	17 (10.25-29)
% Adeq.	75 (53-162)	94 (62.50-147.50)	87.50 (54.50-148)
Cholesterol (mg)	148 (115-197)	147 (114-220)	147.50 (116-211.75)
% Adeq.	60 (53-98)	61 (48-96.50)	60.50 (49.50-97.50)

LT: Liver transplant. Adeq: Adequacy. CW: Current weight. Vit. A: Vitamin A. Vit. C: Vitamin C.
Data expressed as median (interquartile range).

for an assessment of muscle and adipose reserves, while BMI do not differentiate between these two types of tissue. This distinction may have been responsible for the variability and discordance between the different methods of assessing patient nutritional status.

On the other hand, it was still possible to conclude that the patients for whom a longer time had elapsed since their LT had more adequate AC measurements than those who had been recently transplanted. Over time, renal transplanted female patients presented higher AC values in a previously study.[32] In the initial post-LT period, the surgical trauma has been found to lead to an increased catabolic rate,[33] while in the late post-LT period, weight gain appears to be more common.[4] The data in the present study were in accordance with other studies in the literature, and suggested that AC is more adequate over time.

The prevalence of dyslipidemia in the present study was elevated, and significantly higher than that reported in other studies which assessed patients with a longer time post-LT.[34,35] Studies suggest that dyslipidemia is associated with the development of non-alcoholic fatty liver disease in the year following the transplant,[36] and that it may be the greatest risk factor for cardiovascular diseases and mortality in these individuals.[26] A high prevalence of insulin resistance has also been reported in patients who were 7 to 17 years post-LT.[24] However, a separate study also observed a prevalence of insulin resistance of 38% in hepatitis C patients who were approximately[37] 4 years post-LT, using a HOMA-IR cutoff score of 2.5. Some authors also suggest that insulin resistance may be more common in hepatitis C as compared to other etiologies, and is associated with progressive fibrosis and a smaller antiviral response.[7,38] Corticosteroids, tacrolimus, cyclosporin and sirolimus have been shown to be associated with the development of dyslipidemia and insulin resistance.[39] Therefore, it is possible that the use of multiple immunosuppressants may have contributed to the prevalence of dyslipidemia and insulin resistance in the present sample.

The dietary assessment indicated that most patients had adequate nutrient levels. A cross-sectional study using 3-day records and dietary history to assess dietary intake found that post-LT patients had low levels of calories, dietary fiber, vitamin A and calcium, as well as adequacy for cholesterol, all of which is in agreement with the present findings; however, the present results regarding the adequacy of protein, vitamin C, zinc and iron differed from those obtained by other studies.[28] A cohort study involving 7-day dietary records also demonstrated that, although post-LT patients reported inadequate calorie and protein intake, these values were still higher than those reported in the pre-transplant period.[27] However, a distinct cross-sectional study involving dietary history has also found some reports of excessive calorie intake among these individuals.[5] The variability in the methods used to assess dietary intake limits comparisons between the results of different studies.

Our results demonstrated that a longer time post-transplant was correlated with lower vitamin A intake, lower vitamin A adequacy as well as a lower caloric adequacy compared to those with shorter time post-LT. It is important to note that vitamin A regulates immune functioning,[40] so that, given the increased immune vulnerability of post-LT patients caused by the use of immunosuppressants,[41] the maintenance of adequate vitamin A is especially important following LT. Studies of patients at 6 months post-LT have reported the occurrence of low vitamin A intake and an increased oxidative stress and inflammation.[42] Furthermore, vitamin A deficiency is endemic in Brazil.[43] These may have contributed to the results obtained in the present study.

Although the 24-hour dietary recall may not be representative of usual dietary intake due to intra-individual variability, it allows for an investigation of the average intake of groups.[44] Furthermore, studies suggest that a higher BMI, female gender, socioeconomic and education levels, smoking, diet, psychological factors and dietary habits are associated with misreporting, without significant difference between the methods of weighed food record and estimated food record.[45] The correlation between lower caloric intake observed and a longer time post-transplant may therefore counterbalance the relationship between the latter variable and the higher adequacy of AC measurements and a higher prevalence of overweight. Nevertheless, the limitations associated with the 24-hour dietary recall may have influenced the present results.

The small sample size, the cross-sectional design and the fact that not all participants underwent biochemical testing are the main limitations of the present study. The use of the time since the transplant as a selection criterion may have also restricted the sample size. Patients were only assessed at a minimum of 1 month post-transplant since, during this period, many of the patients still have drains in place, are not back on their normal diet, or are still hospitalized. However, it is important to assess patients within the first 2 years post-transplant so as to allow for the early detection of changes in nutritional status and cardiovascular risk. In spite of these limitations, it was possible to detect a high prevalence of dyslipidemia and insulin resistance in post-LT patients, which indicate the presence of significant cardiovascular risk factors in these individuals. These results should be confirmed in larger samples, so as to confirm their generalization to the population.

Conclusion

There is significant variability in the nutritional diagnosis of post-LT patients depending of the anthropometric measurements used. WC assessments indicate that these patients have a high risk of metabolic complications, and biochemical tests show that they also have dyslipidemia and insulin resistance. The prevalence of cardiovascular risk factors underscores the need for transdisciplinary assessments of these populations, and for the development of strategies to improve nutritional status and, therefore, reduce patient risk factors. However, further studies involving higher samples are still required to confirm the present results.

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Conflicts of interest

The authors declare no conflicts of interest.

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