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ORIGINAL ARTICLE

# Obesity, dynapenia and high cardiovascular risk co-exist in post-liver transplant setting: results of a cross-sectional study

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**KEYWORDS**
liver transplantation;
carotid intima-media thickness;
atherosclerotic plaque;
metabolic profile;
dynapenia;
nutritional assessment

**Summary**
*Background:* Cardiovascular disease is a major cause of death in post-liver transplantation (LT). The aim of this study was to evaluate LT patients as to the carotid intima-media thickness (CIMT) and its association with nutritional status, dietary intake, metabolic profile and cardiovascular risk factors.
*Methods:* In this cross-sectional study, adult patients with more than 12 months of post-transplant follow-up underwent clinical, laboratory, functional and nutritional evaluation by 3-day-diet-record, anthropometry and dynamometry. CIMT was evaluated by Doppler ultrasonography.
*Results:* Sixty-nine post-LT patients [males 61%, median of age 59 (51—64) years were included; median time post-liver transplantation 2.8 (1.4—6.3) years]. High prevalence of malnutrition was found (45% of arm muscle area < p15 and 71% of handgrip strength < p30). Excess weight was present in 72% of patients, body mass index $\geq 30\,kg/m^2$ in 35% and metabolic syndrome in 51%. Abnormal CIMT was found in 54% of the sample. Patients with abnormal CIMT presented

*Abbreviations:* AC, arm circumference; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AMA, arm muscle area; AST, aspartate aminotransferase; ASCVD, Atherosclerotic Cardiovascular Disease; BMI, body mass index; BP, blood pressure; CIMT, carotid intima-media thickness; CP, carotid plaque; CV, cardiovascular; GGT, gamma glutamyl transferase; GI, glycemic index; GL, glycemic load; HDL, HDL cholesterol; HS, handgrip strength; hs-CRP, high-sensitive C-reactive protein; IPAQ, International Physical Activity Questionnaire; LDL, LDL cholesterol; LT, liver transplantation; METs, metabolic equivalent task/week; MS, metabolic syndrome; TC, total cholesterol; TG, triglyceride; TS, triceps skinfold; WC, waist circumference.

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higher cardiovascular risk Score, LDL cholesterol, higher prevalence of high-sensitive C-reactive protein $\geq$ 1 mg/L and higher intake of saturated and trans fatty acids ($P < 0.05$ for all).
*Conclusions:* Abnormal IMT was commonly found in LT patients presenting at the same time with overweight and dynapemia. These results were associated with higher LDL-cholesterol levels, high-sensitive C-reactive protein $\geq$ 1 mg/L and higher intake of saturated and trans fatty acids. Preventive measures, including dietary advice, are required for all post-liver transplantation patients to minimize cardiovascular risk.


## Introduction

Advances in medical and surgical treatment led to an increase in long-term survival after liver transplantation (LT). Currently, LT reaches a median survival of nearly 90% at 01 year and, 75% at 5 years post-LT [1,2]. Conversely, due to longer LT survival, some complications have emerged, such as metabolic syndrome (MS) and malignancies, which are the main issues to be solved in the long-term care of transplantees [3].

Moreover, the incidence of cardiovascular (CV) disease has increased in the last few years in LT patients. CV complications are among the top three causes of death in post-LT patients, including heart, cerebrovascular and peripheral vascular disease [1,2]. This is possibly associated with metabolic complications in the post-transplant period, such as increased incidence of obesity, sedentary lifestyle and glucose and lipid metabolism disorders, together with the chronic inflammation underlying the LT [3,4].

The progression of active liver disease as well as the post-transplant period is marked by important and distinct nutritional changes. In advanced liver disease, patients present major malnutrition, with dietary restriction, weight loss and also dynapenia (designation of loss of muscle strength not related to muscular or neurologic disease), highly associated with mortality [5,6]. This condition is partly reversed after LT, when patients return to previous dietary habits, which possibly contribute to an exaggerated weight gain and metabolic impairments.

In order to assess atherosclerotic cardiovascular risk, prediction risk scores have been frequently applied. The atherosclerotic cardiovascular disease (ASCVD) risk Score developed by the American College of Cardiology and the American Heart Association is a sex- and race-specific single multivariable risk assessment tool used to estimate the 10-year CV disease risk that has clinically replaced the Framingham risk score [7]. It is based on sex, age, smoking, systolic blood pressure (BP), total cholesterol (TC), HDL cholesterol, diabetes and treatment for hypertension.

It is well established that both arterial stiffness and atherosclerosis are important preclinical stages of CV disease [8]. Therefore, ultrasonographic measurement of arteries to assess the carotid intima-media thickness (CIMT) as well as the presence of a carotid plaque (CP) has been considered a useful method for CV risk reclassification in clinical practice [9,10].

Considering the concern related to cardiovascular disease and nutritional changes, we believe that it is important to investigate cardiovascular risk and nutritional status in LT patients. Thus, the aim of this study was to evaluate LT patients as to CIMT and its association with nutritional status, food intake, metabolic profile and CV risk factors such as MS and ASCVD risk Score.

## Materials and methods

This cross-sectional study included adult transplanted patients treated at an outpatient clinic of the Gastroenterology Division of Hospital de Clínicas de Porto Alegre, Brazil, from July, 2014 to April 2016. Patients with post-LT follow-up less than a 12-month period were not included, because it is considered that the transplantation patient is clinically more stable and adapted to a new life condition only one year after this takes place. Also, patients with post-LT chronic kidney disease were not included because their nutritional status is usually affected and, moreover, they need specific dietary restrictions that could influence the results of diet records and nutritional assessment. Patients that have undergone highly urgent liver transplantation, as in cases of acute liver disease and liver graft loss (retransplantation) were also not included.

The Ethics and Research Committee at HCPA approved the protocol, and patients were included only after reading, understanding and signing an Informed Consent Form. All evaluations were performed on the same day, except for the Doppler ultrasonography, diet records (that patients fill in at home) and the laboratory assessment that were performed within the approximately 3-week period.

### Anthropometric assessment

Body mass index (BMI), conicity index and arm muscle area (AMA) were estimated through measurements of body weight, height, waist circumference (WC), arm circumference and triceps skinfold. Data before LT, including dry weight, were assessed retrospectively by electronic medical records. Body mass index (BMI), conicity index (CI) and arm muscle area (AMA) were calculated according to pre-established formulas [11,12]. Data before LT, including dry weight, were assessed by electronic medical records.

### Dynapenia assessment

Dynapenia was determined by the handgrip strength (HS) of the non-dominant hand by dynamometry, using a Jamar® mechanical dynamometer. Patients were positioned sitting down with a straight back and no armrests and with elbow flexion at 90º. The test was repeated three times at 1-minute intervals and the maximum score recorded was used for analysis. Results were compared to reference values found in the study of Schlüssel et al. [13,14].

### Sarcopenia criteria

According to the European consensus [15], sarcopenia was considered as the presence of both low muscle mass and low muscle strength (dynapenia). Low muscle mass was defined as AMA below percentile 15, and dynapenia as HS below 30 kgf and 20 kgf for men and women respectively.

### Laboratory assessment

Blood samples were obtained after a 12-h fast, after inclusion in the study. The tests included were: total cholesterol (TC), HDL cholesterol (HDL), LDL cholesterol, triglyceride (TG), glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), albumin, and high-sensitive C-reactive protein (hs-CRP).

### Dietary intake assessment

The patient's usual diet was assessed by 3-day-diet-record (two non-consecutive weekdays and one-weekend day). Macro-, micronutrients and calories were assessed using the NutriBase 2007 software (Clinical Nutrition Manager v.7.14; Cybersoft). Nutrient data were expressed in raw amounts (g/day, mg/day mcg/day or IU/day) or in grams per kilogram of body weight. The dietary glycemic index (GI) was estimated by the weighted GI value of each consumed food and expressed as percentage. Dietary glycemic load (GL) was calculated as the product of dietary GI and total carbohydrate intake divided by 100, using glucose as reference food.

### Physical activity assessment

Habitual physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) long form. From IPAQ it was possible to determine the level of physical activity and the weekly energy expenditure, expressed by metabolic equivalent task/week (METs). Less than 600 METs were considered low physical activity.

### Blood pressure measurement

Blood pressure (BP) was measured twice using a digital sphygmomanometer after 10 minutes of rest, with patients in the sitting position.

### Cardiovascular risk score

Atherosclerotic Cardiovascular Disease (ASCVD) risk Score was used to estimate the 10-year risk of developing a first ASCVD event. This score includes the following variables: sex, age, systolic BP, CT, HDL, diabetes, treatment for hypertension and smoking. An ASCVD risk score higher than 7.5% was considered as high CV risk [7].

### Metabolic syndrome

MS were considered according to the consensus statement of the International Societies [16].

### Carotid intima-media thickness and plaque

Doppler ultrasonography of carotid arteries was performed to measure the CIMT and/or to detect the presence of CP. According to the Mannheim Carotid Intima-Media Thickness and Plaque Consensus [10] and Brazilian Cardiology Society [17], CIMT was considered increased when > 1.0 mm, and presence of CP was defined as focal structures encroaching at least 0.5 mm into the arterial lumen or 50% of the surrounding CIMT value, or demonstrated CIMT > 1.5 mm. This examination was performed by a single vascular medicine specialist. Patients with an abnormal carotid (increased CIMT or CP) are at increased CV risk, so they were grouped for analysis and compared with patients with a normal carotid.

### Statistical analysis

Statistical analysis was performed using PASW Statistics software. Variables with a normal distribution were expressed as mean ± SD, and asymmetrically distributed data were presented as median and interquartile range. Comparisons were analyzed by Student's *t*-test or Mann-Whitney's *U*-test for continuous variables, and by $Chi^2$ test for categorical variables. Pearson or Spearman correlation coefficients were used for bivariate correlation. Multivariate analysis was performed by Poisson regression with robust variance. The regression model included selected variables with a *P*-value < 0.25 in univariate analysis and manual backward elimination of non-significant variables. *P*-values < 0.05 were considered statistically significant.

## Results

Initially, 72 post-LT patients were enrolled. Since 3 of them had a history of a CV event after LT, they were excluded from analyses. Therefore, our sample consisted of 69 patients, who were mostly Caucasian (92.7%). The main causes of liver disease in these patients were hepatitis C virus (68.1%) and alcoholic cirrhosis (23.2%). Most of them had received tacrolimus-based immunosuppression (87.0%).

Clinical, anthropometric and metabolic profiles of post-LT patients according to CIMT are shown in Table 1. A considerable prevalence of malnutrition, loss of strength and protein/muscle depletion (sarcopenia) was found according to HS (dynapenia) and AMA. Dynapenia was found

**Table 1** Clinical, anthropometric and metabolic profiles of post-liver transplantation patients according to carotid intima-media thickness.

| | Normal CIMT | Abnormal CIMT[d] | *P*-value |
|---|---|---|---|
| N | 32 | 37 | |
| Gender (% male) | 59.4 | 62.2 | 0.813[a] |
| Age (years) | 55 (48—64) | 61 (57—65) | 0.059[b] |
| Years after LT | 1 (4—9) | 2 (1—4) | 0.055[b] |
| Smoking history (%) | 43.7 | 67.7 | 0.055[a] |
| Weight gain (kg) | 13.3 ± 10.7 | 8.1 ± 10.0 | **0.039**[c] |
| BMI < 60 y (kg/m$^2$) | 28.4 (26.3—34.7) | 27.6 (23.7—32.3) | 0.521[b] |
| BMI ≥ 60 y (kg/m$^2$) | 29.2 (27.6—34.9) | 26.6 (24.8—29.9) | 0.058[b] |
| WC (cm) | 103.1 ± 15.1 | 101.2 ± 11.4 | 0.549[c] |
| Increased WC (%) | 65.6 | 59.5 | 0.627[a] |
| Conicity index | 1.34 | 1.35 | 0.404[c] |
| HS < P30 (%) | 62.5 | 78.4 | 0.187[a] |
| HS < P10 (%) | 50.0 | 56.8 | 0.633[a] |
| Dynapenia (%) | 62.5 | 70.3 | 0.610 |
| Sarcopenia (%) | 28.1 | 37.8 | 0.450 |
| AMA < P15 (%) | 37.5 | 51.3 | 0.333[a] |
| Systolic BP (mmHg) | 125.6 ± 13.4 | 125.1 ± 12.2 | 0.882[c] |
| Diastolic BP (mmHg) | 76.2 (70.6—80.9) | 76.5 (71.7—80.2) | 0.993[b] |
| TC (mg/dL) | 152 (130—177) | 168 (155—194) | 0.065[b] |
| LDL (mg/dL) | 72.1 ± 35.7 | 101.9 ± 39.1 | **0.014**[c] |
| HDL (mg/dL) | 41 (35—60) | 48 (36—62) | 0.647[b] |
| TG (mg/dL) | 114 (89—151) | 100 (78—167) | 0.475[b] |
| Glucose (mg/dL) | 99 (90—116) | 99 (90—114) | 0.471[b] |
| hs-CRP[d] | 1.10 (0.27—3.43) | 2.35 (1.26—3.39) | 0.064[b] |
| hs-CRP ≥ 1 mg/L (%)[e] | 50.0 | 79.4 | **0.018**[a] |
| Albumin (g/dL) | 4.4 ± 0.3 | 4.2 ± 0.4 | 0.111[c] |
| ALT (U/L) | 36 (25—57) | 36 (23—72) | 0.964[b] |
| AST (U/L) | 30 (22—57) | 38 (22—56) | 0.544[b] |
| GGT (U/L) | 86 (45—199) | 94 (42—263) | 0.818[b] |
| ALP (U/L) | 96 (82—152) | 99 (90—144) | 0.993[b] |
| MS (%) | 59.4 | 43.2 | 0.230[a] |
| High CV risk (%)[f] | 50.0 | 78.4 | **0.022** |
| METs | 2410 (661—4314) | 1782 (1020—3531) | 0.749[b] |

Results presented as %; median (p25—p75) or mean ± SD.
CIMT: carotid intima-media thickness; LT: liver transplantation; BMI: body mass index; WC: waist circumference; HS: handgrip strength; AMA: arm muscle area; BP: blood pressure; TC: total cholesterol; HDL: HDL cholesterol; LDL: LDL cholesterol; TG: triglycerides; hs-CRP: high-sensitive C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma glutamyl transferase; ALP: alkaline phosphatase; MS: metabolic syndrome; ASCVD: atherosclerotic cardiovascular disease; METs: MET-minute/week.
[a] Qui$^2$ test.
[b] Mann—Whitney—Wilcoxon *U*-test.
[c] Student's *t*-test.
[d] Increased CIMT + CP.
[e] Excluded those with hs-CRP ≥ 10 mg/L.
[f] ASCVD risk Score ≥ 7.5%.

in 66.7% of patients. Half of the patients with dynapenia also had sarcopenia. Although 85.2% of the women presented dynapenia, sarcopenia was found only in 14.8%. Men presented a higher prevalence of sarcopenia and lower prevalence of dynapenia ($P = .017$ both).

The proportion of AMA below percentile 15 was higher in the male than female gender (83.9% vs. 16.1%; $P < .001$), moreover 30.9% of males are below percentile 5 which indicates severe malnutrition. A positive correlation was detected between HS and METs ($r = .271$; $P = .024$). In contrast, a large number of obese was detected in this population. The majority of patients (81.1%) gained weight after LT, and it was positively correlated with years after LT ($r = .284$; $P = .018$). Data from dietary intake according to CIMT are presented in Table 2.

Estimated associations related to abnormal CIMT outcome are presented in Table 3. Age ≥ 60 years, hs-CRP ≥ 1 mg/L and trans fatty acid intake ≥ 1% of daily calories were independent predictors of abnormal CIMT.

More than half (50.7%) of the post-LT patients presented with MS. The proportion of MS components is shown in Fig. 1. MS was positively associated with weight gain after LT ($P = .040$) and years after LT ($P = .005$).

**Table 2** Daily dietary intake of post-liver transplantation patients according to carotid intima-media thickness.

| | Normal CIMT | Abnormal CIMT[c] | *P*-value |
|---|---|---|---|
| N | 32 | 37 | |
| Energy (kcal/kg) | 23.8 (12.3—50.7) | 27.0 (10.8—49.2) | 0.084[a] |
| Carbohydrates (g/kg) | 2.86 ± 1.07 | 3.39 ± 1.20 | 0.062[b] |
| Protein (g/kg) | 1.22 (0.33—3.27) | 1.21 (0.51—2.38) | 0.950[a] |
| Lipid (g/kg) | 0.95 (0.48—1.92) | 1.01 (0.33—2.21) | 0.106[a] |
| Saturated FA (g/kg) | 0.28 ± 0.11 | 0.35 ± 0.16 | **0.032** |
| Monounsaturated FA (g/kg) | 0.29 (015—0.72) | 0.38 (0.23—0.45) | 0.119[a] |
| Polyunsaturated FA (g/kg) | 0.24 (0.09—0.46) | 0.21 (0.06—0.62) | 0.691[a] |
| Trans FA (g/kg) | 0.000 (0.000—0.015) | 0.002 (0.000—0.220) | **0.011**[a] |
| Cholesterol (mg) | 250.0 (154.7—316.1) | 255.9 (170.0—313.3) | 0.715[a] |
| Fiber (g/kg) | 21.4 (0.0—46.9) | 20.3 (8.1—52.3) | 0.623[a] |
| Glycemic index (%) | 59.5 ± 5.6 | 56.7 ± 7.0 | 0.069[b] |
| Glycemic load (g) | 106.9 ± 42.9 | 111.8 ± 44.3 | 0.641[b] |

Results presented as median (min—max) or mean ± SD.
FA: fatty acids. Characters in bold: P < 0.05.
[a] Mann—Whitney—Wilcoxon *U*-test.
[b] Student's *t*-test.
[c] Increased CIMT + CP.

**Table 3** Adjusted prevalence ratio and respective confidence interval (95% CI) of abnormal carotid intima-media thickness according to age, hs-CRP, and trans fatty acids intake.

| Variables | PR | 95% CI | *P*-value |
|---|---|---|---|
| Age > 60 y | 1.590 | 1.021—2.478 | 0.036 |
| hs-CRP ≥ 1 mg/dL | 1.052 | 1.005—1.101 | 0.039 |
| Trans FA ≥ 1% | 1.884 | 1.007—3.525 | 0.003 |

Robust Poisson regression model.
PR: prevalence ratio; CI: confidence interval; hs-CRP: high-sensitivity c-reative protein; y: years; LT: liver transplantation; FA: fatty acids.

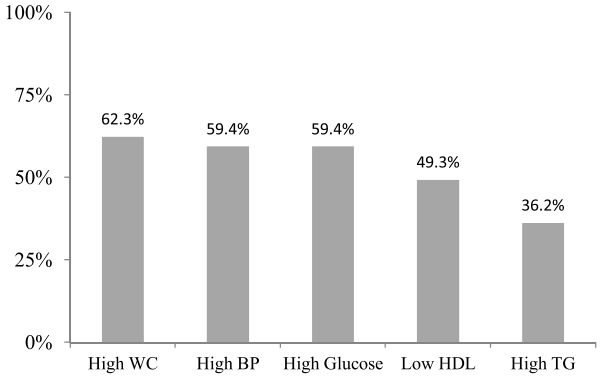


**Figure 1** Proportion of components of metabolic syndrome in post-liver transplantation patients High WC: waist circumference > 88 for female and > 102 for male; High BP: systolic blood pressure ≥ 130 and/or diastolic BP ≥ 85 mmHg or antihypertensive drug treatment; High glucose: glucose ≥ 100 mg/dL or insulin or hypoglycemic drug treatment; Low HDL: HDL cholesterol < 40 mg/dL for male and < 50 mg/dL for female or drug treatment for reduced HDL; High TG: triglycerides ≥ 150 mg/dL or drug treatment for elevated triglycerides.

According to the ASCVD risk score, 65.2% of patients were at high CV risk. A ASCVD risk Score higher than 7.5 was associated with the presence of MS (*P* = .045), higher trans fatty acids intake (*P* = .025), higher conicity index (*P* = .007), but lower weight gain post-LT (*P* = .037) compared to those with low CV risk.

Still concerning CV risk, a prevalence was found of 43.5% of patients with CP, associated with ASCVD risk score (*P* = .010). CIMT was weakly correlated with ASCVD (*r* = .280; *P* = .020).

Patients who had undergone LT more than 2 years previously, seemed to have a worse metabolic profile, such as higher systolic and diastolic BP and WC (*P* < .040 for all), a trend for higher fasting glucose (*P* = .054) and BMI (*P* = .052), and also, a higher prevalence of MS (*P* = .025). A negative correlation was found between albumin and hs-CRP (*r* = —.292; *P* = .015).

## Discussion

To the best of our knowledge, the present study is surprisingly the first to document the CIMT measurement in adults post-LT. We found a high prevalence of patients with increased CIMT and CP, and MS. Patients with abnormal CIMT presented a worse metabolic profile, especially lipid and inflammatory. Moreover, an increased intake of saturated and trans fatty acids was observed in these patients.

In this study, post-LT patients presented a high prevalence of dynapenia, especially in women. It is well described that muscle wasting from metabolic abnormalities of cirrhosis still persists after LT [18]. It is interesting to note that the prevalences of the indicators of malnutrition evaluated in this study differed between genders. On the other hand, obesity was also highly prevalent in this population. Anastácio et al., reported that 53% of patients weighed more than their weight before liver disease within one year after LT, which corroborated the impression that the weight gain

after LT corresponds to an increase of fat mass, besides the recovery of their nutritional status after liver disease [19].

Similarly to our results considering all patients, Richards et al. described a median weight gain of 9.5 kg and a prevalence of 30.6% of obesity (BMI $\geq$ 30 kg/m$^2$) 3 years after LT [20]. The excessive weight gain after LT is concerning, because it would increase the risk of MS and its associated complications, such as diabetes, CV disease, renal disease, and de novo NASH in the graft. The reasons why patients gain weight and lots of them become obese after LT have not been elucidated, but it is believed that it could be a result of immunosuppression and overeating after recovering their appetite and prior eating habits after a long period of restrictions. These findings highlight the fact that nutritional monitoring is important immediately after LT, since the changes in weight happen soon [3].

Substantial prevalence of MS has been described before. A Brazilian study with 148 post-LT patients also found 50% of MS in post-LT, although using different WC criteria from ours [21]. Our study observed an association between MS, weight gain and years after LT. In agreement with that, a previous study showed that the prevalence of MS was 38.8% at 1 year after LT and increased between 44% and 45% after 3 to 5 years, and it was associated with the increase in BMI [22].

According to the ASCVD risk score, our study found that more than half of the patients were at higher CV risk and it was associated with abnormal CIMT. However, 16 (35.5%) patients classified as low CV risk by the score presented abnormal CIMT.

Few studies have accessed CV risk in post-LT patients using this updated equation, proposed by the American College of Cardiology and the American Heart Association. Very recently, a new prediction model for cardiovascular risk in orthotopic LT patients was proposed, but it has some limitations (the model only included preoperative risk factors) and still requires further validation in different centers [23].

Comparing patients according to abnormal CIMT, even though many studies have described a close association between MS and its components [24—26], we did not identify a significantly worse metabolic profile in the patients with abnormal CIMT, except for LDL, which was higher. It agreed with Kozakova et al. and Leng et al. who also found a higher LDL without difference in other blood lipids, in subjects with CP [27,28]. Contributing to this, a study with young adults demonstrated that apolipoprotein B, which is the main protein in LDL, increased the relative risk of abnormal CIMT [24]. It is interesting to note that median levels of LDL found in LT-patients with abnormal CIMT, are still near/below optimal levels related to potential atherogenicity.

The conicity index, proposed as a model to assess primarily the body fat distribution, gives greater importance to abdominal obesity. The association between conicity index and ASCVD risk Score found in our study is in agreement with other studies that describe the conicity index as a better predictor of CV risk, comorbidities associated with CV disease and coronary artery disease than other parameters of obesity [29,30]. Even though our study has shown that patients with abnormal CIMT gained more weight post-LT, than patients with normal CIMT, it does not impact weight, BMI, and other body measurements.

Surprisingly, the patients with abnormal CIMT presented lower indicators of obesity. Interestingly, a study of obese subjects that evaluated CIMT and body composition by dual-energy X-ray absorptiometry concluded that lean mass, and not fat mass, might contribute to increase CIMT, and, the explanation can be that increasing lean mass may influence the CV phenotype, leading to a small increase in CIMT [31]. In LT, Pisano et al., in a recent review, presented preliminary data that describe a progressive increase of CIMT starting as early as the 6th month post-LT, and similar prevalence of CP pre- and post-LT [32].

Our multivariable regression model confirmed age as an independent predictor of abnormal CIMT. This result is not surprising since age is a well-known traditional non-modifiable risk factor. It has been assumed that the contribution of age in multivariable models is a reflection of the intensity and the duration of exposure to the traditional risk factors [33].

Nowadays, the role of inflammation in the progression of CV disease is much discussed and it is especially important after LT. Alvares-da-Silva et al. demonstrated that LT recipients present higher levels of pro-inflammatory cytokines and endothelial biomarkers than controls, highlighting the influence of inflammation on CV disease [4]. The same group showed similar results before studying a sample of HCV non-cirrhotic patients [34]. The circulating marker of inflammation hs-CRP appears to contribute to the identification of people at risk of developing CV disease. In this study we demonstrated that levels of hs-CRP $\geq$ 1.0 mg/L (that also reflect CV risk and chronic low-grade inflammation) are a predictor of abnormal CIMT. Besides, we found a significantly higher prevalence of patients with hs-CRP $\geq$ 1.0 mg/L and a trend to higher median values of hs-CRP in patients with abnormal CIMT. It corresponds to a several studies which observed the association between increased CIMT and increased levels of hs-CRP [35], however the relationship between hs-CRP and CIMT progression is still controversial.

It has been already proved that saturated and trans fatty acids are associated with increased CIMT in epidemiological studies [36]. Concurring with that, our post-LT patients with abnormal CIMT and also those with high CV risk according to ASCVD risk score also demonstrated a higher intake of those fatty acids. Also, considering that international dietary guidelines recommend a daily intake of trans fatty acids limited to 1% of daily caloric intake or as low as possible, we also indicated that an intake higher than that was a predictor of abnormal CIMT [37,38]. Concerning CV disease, studies have proposed that the adoption of a Mediterranean diet and replacing saturated fatty acids, trans fatty acids and carbohydrates by polyunsaturated fatty acids would be associated with a lower risk of CV disease [39].

We have to acknowledge some limitations in the present study. First, we grouped abnormal CIMT and CP together to compare them with normal CIMT. We did not expect to find such a large proportion of patients with CP, as the median time after LT is not much longer. We know that CIMT and CP are different structures regarding localization, natural history and predictive value for vascular events, but both share common risk factors for atherosclerosis [10]. Besides, increased CIMT has been considered a predictor of CP and might occur in an earlier phase of the atherosclerotic process [40]. Therefore, we believe that both increased CIMT

and CP are at higher CV risk than those with normal CIMT. We did not have access to a metabolic profile before LT to determine if patients really developed MS after LT. Also, the weight before LT was taken from medical records, and it could have been measured at different moments. Due to the instrument used to assess physical activity, we believe that there may have been an overestimation caused by the Domestic and Garden (Yard Work) domain, concealing patients with a low level of physical activity.

In conclusion, this study showed a high prevalence of an abnormal CIMT in a sample of overweight and sarcopenic LT patients. Abnormal CIMT was associated with higher ASCVD risk Score, higher LDL-cholesterol levels, hs-CRP $\geq$ 1 mg/L and higher intake of saturated and trans fatty acids. It is necessary to provide strong preventive measures, including improvement of dietary quality, for all post-LT patients in order to minimize the risk of CV disease in the future.

## Authorship

Bruna Cherubini Alves: concept/design, data analysis/interpretation, drafting article, statistics, data collection; Juliana Paula Bruch, Clara Belle Manfroi Galinatti and Claudia Czarnobay Garbin: data collection and statistics; Mário Reis Álvares-da-Silva and Valesca Dall'Alba: concept/design, data analysis/interpretation, critical revision of article, approval of article.

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## Disclosure of interest

The authors declare that they have no competing interest.

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