



Impacts and Prevalence of Sarcopenia in Patients with MASLD: A Cross-Sectional Study

Kally Janaína Berleze¹, Luis Fernando Ferreira^{1*}, André Ferreira D'Ávila², Caroline Buss³, Cristiane Valle Tovo¹, Luis Henrique Telles da Rosa⁴

¹Postgraduation program in Medicine: Hepatology, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Brazil; ²Postgraduation program in Pathology, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Brazil; ³Department of Nutrition, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Brazil; ⁴Department of Physiotherapy, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Brazil

ABSTRACT

Introduction: Sarcopenia, muscle loss, often coexists with MASLD, a common liver disorder, which is more prevalent in those with sarcopenia. Sarcopenia also increases the risk of liver conditions like steatosis and fibrosis. Studies on sarcopenia in MASLD are common in developed countries, but fewer follow the EWGSOP2 guidelines in Brazil.

Aim: To assess sarcopenia prevalence in MASLD patients.

Methods: Cross-sectional study conducted at the Gastroenterology/Hepatology Service of ISCMPA with patients diagnosed with MASLD. The EWGSOP2 criteria were used to evaluate sarcopenia. Categorical data presented as absolute and relative frequency; parametric continuous data expressed as mean \pm standard deviation; non-parametric continuous data as median and IQR. Gender differences in were analyzed using Fisher's Exact Test or Chi-squared tests, and for continuous variables, T student tests (parametric) and Mann-Whitney U tests for independent samples (non-parametric). The significance level was set at 5% ($p < 0.05$).

Results: The study involved 103 MASLD patients with an average age of 60.39 years, comprising 48 (46.60%) adults and 55 (53.40%) older individuals. Concerning sarcopenia diagnosis, four individuals exhibited decreased muscle strength; two had reduced MME (sarcopenia); and one showed decreased walking speed (severe sarcopenia). Among the participants, 63 (60.6%) were physically active. 35 (62.5%) had mild to moderate steatosis, while 21 (37.5%) had severe steatosis. In terms of EHNA, 13 subjects (24.08%) had moderate to severe EHNA. Regarding fibrosis classification, 68 (72.34%) individuals had undetermined or high probability based on the NAFLD score, with higher prevalence in males ($n=23$; 88.5%). Fibrosis assessment *via* liver biopsy revealed 27 (28.72%) in F1 and F2 and 15 (16.96%) in F3 and F4. Stratification of fibrosis into F3 and F4 was more common among men ($n=9$; 47.4%).

Conclusion: Most of the population was physically active. The parameters indicating sarcopenia exceeded the thresholds recommended by EWGSOP2. The prevalence of sarcopenia was low in individuals with MASLD.

Keywords: Sarcopenia; MASLD; Liver Disease; Aging

Correspondence to: Luis Fernando Ferreira, Post-graduation program in Medicine: Hepatology, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Brazil, E-mail: proffernandof@gmail.com

Received: 03-Nov-2023, Manuscript No. JCRB-23-23730; **Editor assigned:** 06-Nov-2023, Pre QC No. JCRB-23-23730 (PQ); **Reviewed:** 20-Nov-2023, QC No JCRB-23-23730; **Revised:** 27-Nov-2023, Manuscript No. JCRB-23-23730 (R); **Published:** 06-Dec-2023, DOI: 10.35248/2155-9627.23.S17.001.

Citation: Berleze KJ, Ferreira LF, D'Ávila AE, Buss C, Tovo CV, da Rosa LHT (2023) Impacts and Prevalence of Sarcopenia in Patients with MASLD: A Cross-Sectional Study. J Clin Res Bioeth. S17:001.

Copyright: © 2023 Berleze KJ, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

INTRODUCTION

Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) is one of the most common metabolic liver disorders, becoming the predominant cause of chronic liver disease, with an estimated worldwide prevalence of approximately 25%, and its incidence is rapidly increasing [1-3]. MASLD comprises a broad spectrum of diseases, including simple steatosis, Non-Alcoholic Steatohepatitis (NASH), fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma [4]. Globally, the prevalence of NAFLD is rising due to an increasingly sedentary lifestyle, the globalization of the Western diet, and the growing frequency of obesity, Insulin Resistance (IR), Type 2 Diabetes Mellitus (T2DM), and dyslipidemia [5].

Sarcopenia and MASLD share some pathophysiological mechanisms, with IR consistently associated with both conditions. The primary pathophysiology of sarcopenia is linked to insulin resistance, which plays a pivotal role in the development of MASLD. The prevalence of sarcopenia is higher in patients affected by NAFLD and correlates with the severity of MASLD [6]. Sarcopenia is a progressive and widespread skeletal muscle disorder associated with an increased likelihood of adverse outcomes, including falls, fractures, physical disability, and mortality [7]. While sarcopenia has been linked to aging, its development is now recognized earlier, with various factors contributing to its development beyond aging, often being associated with multisystem disorders, including MASLD [8]. These insights have implications for interventions aimed at preventing or delaying the development of sarcopenia.

In a recent meta-analysis, the risk of MASLD and MASLD-related fibrosis was higher in individuals with sarcopenia than in those without sarcopenia (29% and 57%, respectively) [9]. In general, sarcopenia is associated with an increased risk of hepatic steatosis, NASH, and advanced fibrosis [10]. Muscle loss is related to reduced survival, longer hospital stays, and mortality in cirrhotic patients [11]. Furthermore, muscle function is interconnected with MASLD, and *vice versa*.

The prevalence of sarcopenia in patients with MASLD has been investigated in clinical studies conducted in populations of developed countries following the first consensus of the European Working Group on Sarcopenia in Older People (EWGSOP), with few Brazilian studies on patients with MASLD in accordance with the guidelines of the second consensus (EWGSOP2) [12].

The objective of this study was to determine the prevalence of sarcopenia in individuals with MASLD.

MATERIALS AND METHODS

This was a cross-sectional study derived from an observational prospective cohort study involving individuals diagnosed with MASLD who received outpatient care at the Gastroenterology/Hepatology Service of the Santa Casa de Misericórdia de Porto Alegre (ISCMPA).

All patients over 18 years of age with confirmed MASLD, determined by hepatic biopsy or non-invasive methods (imaging), attended at Outpatient Clinic of ISCMPA between

the period of realization, and that signed the ICF, were included. Exclusion criteria encompassed patients with hepatitis B or C viruses, significant alcohol consumption (>20 g/day for women and >30 g/day for men), other causes of chronic liver diseases, secondary causes of MASLD, and patients with hepatocellular carcinoma. The data collection occurred between January-2018 until March-2020 [13-15].

The study received approval from the research ethics committee of the University of Health Sciences of Porto Alegre (UFCSPA) and the Irmandade Santa Casa de Misericórdia de Porto Alegre (ISCMPA) under the reference numbers 1.894.929 and 1.856.118, respectively. Additionally, all patients provided informed consent by signing the Informed Consent Form (ICF). All the procedures followed the declaration of Helsinki, and the Brazilian law of protection of personal data (law 13.709/2018).

Data collection

The collects were made by trained professionals, blinded for the outcomes. The data collected were analyzed by a statistician blinded for all project's information.

Participants underwent a comprehensive medical history assessment, including current and past medical history, socioeconomic status, smoking behavior, alcohol consumption, and ethnicity. For the laboratory assessments, fasting blood samples were collected by personnel from the Clinical Analysis Laboratory of ISCMPA. The following tests were conducted: Glucose and insulin levels, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), albumin, platelets, creatinine, creatine protein, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. From these analytes, insulin resistance and sensitivity markers and the Metabolic Associated Fatty Liver Disease (MASLD) score were calculated.

Insulin resistance was estimated through the Homeostasis Model Assessment (HOMA-IR) calculation, defined as:

$$\text{(fasting insulin (pmol/l)} \times \text{fasting plasma glucose (mmol/l)}) / 22.5.$$

Insulin resistance, based on the HOMA-IR index, was considered when values exceeded 2.71 [16,17]. It was also calculated using the TyG.

$$\text{TyG} = \ln (\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)}) / 2$$

With values greater than 4.55 for women and 4.68 for men indicating insulin resistance [18]. Insulin sensitivity was estimated through the Quantitative Insulin Sensitivity Check Index (QUICK), given by the formula:

$$1 / (\log \text{fasting plasma glucose (mg/dL)} + \log \text{fasting insulin (}\mu\text{U/dL)})$$

There is no specific cutoff point for the QUICK index. However, Katz et al., found the following means and standard deviations: non-obese 0.382 ± 0.007 ; obese 0.331 ± 0.010 ; and individuals with diabetes 0.304 ± 0.007 . Individuals are considered insulin-sensitive when QUICK index values are equal to or greater than these respective values found [19].

For fibrosis evaluation, hepatic biopsy was performed whenever possible, and in other patients, fibrosis was assessed using the MASLD score, calculated using the laboratory tests available at the study's inclusion. Those with a MASLD score indicating intermediate probability (score between -1.455 and 0.675) or high probability (cutoff point >0.675) of hepatic fibrosis were invited to undergo hepatic biopsy [20].

Hepatic biopsy was indicated following the guidelines of the American Association for the Study of Liver Disease (AASLD) (4), which recommend biopsy for patients with MASLD at risk of Non-Alcoholic Steatohepatitis (NASH) and advanced fibrosis as part of a care protocol. Hepatic biopsy was performed using ultrasound-guided Trucut needle technique, and the obtained material was analyzed by a professional with expertise in the field of liver pathology, covering relevant histopathological classifications for MASLD assessment. The histopathological analyses employed the NAFLD Activity Score (NAS), validated by Kleiner et al., and the score created by Bedossa et al., for the evaluation of MASLD in morbidly obese patients [21,22].

Regarding the physical examination, body weight and height were measured to calculate the Body Mass Index (BMI) using the formula weight (kg)/height (m) squared. The nutritional status, according to the BMI, for adult patients (20-59 years and 11 months old) was classified according to the World Health Organization, while elderly patients were classified according to Lipschitz et al., [23]. Waist Circumference (WC) was measured at the mid-point between the last rib and the iliac crest, classified as visceral obesity according to WC measurements specific to ethnicity (cm) for men (M) women (F): Caucasians: ≥ 94 cm (M); ≥ 80 cm (F); South Africans, Western Mediterranean's, and Middle Easterners: same as Caucasians; South Asians and Chinese: ≥ 90 cm (M); ≥ 80 cm (F); Japanese: ≥ 90 cm (M); ≥ 85 cm (F); South Americans and Central Americans: use South Asian references (International Diabetes Federation). These measurements were conducted by trained professionals using previously established and validated procedures [24].

Sarcopenia assessment and diagnosis were conducted following the criteria outlined by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2). Muscle strength was assessed by measuring handgrip strength using a portable dynamometer from JAMAR (JAMAR Hydraulic Hand Dynamometer, SAEHAN Corp, Korea Biometrics Europe BV, Almere, Netherlands) [25-27]. The data was recorded in Kilograms (Kg). The patient's position and test execution adhered to the recommendations of the American Society of Hand Therapy [28].

Total body Skeletal Muscle Mass (SMM) was assessed using Bio-Impedance Analysis (BIA). A Biodynamics model 450 device was employed for BIA measurements. The patient's preparation and positioning followed the protocol proposed by the European Society for Clinical Nutrition and Metabolism [29]. The collected data was impedance resistance, and SMM was

calculated using the formula proposed by Janssen et al., [30]. Additionally, the Skeletal Muscle Mass Index (SMI) was calculated by dividing height by weight squared (Kg/m^2).

Physical performance was evaluated through the usual gait speed, using the six-minute walk test conducted according to the recommendations of Janssen et al., [30]. The data was obtained by dividing the meters covered by 360 seconds (six minutes). The level of physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) [31].

Statistical analysis

The sample was collected by convenience from the outpatient clinic at the Gastroenterology/Hepatology Service of ISCMPA.

For descriptive analysis, categorical data were presented as absolute (n) and relative (%) frequency, while parametric continuous data were expressed as mean \pm standard deviation, and non-parametric continuous data were presented as median (interquartile range). To test gender differences in categorical variables, Fisher's Exact Test or Chi-square tests were used, and for continuous variables, independent samples t-tests (parametric) and Mann-Whitney U tests (non-parametric) were applied. The analysis was conducted using the Statistics Package for the Social Sciences, version 22, with a significance level of 5% ($p < 0.05$).

RESULTS

The study included 103 patients with MASLD, comprising 48 (46.6%) adults and 55 (53.4%) older individuals. The average age of the population was 60.39 years. Table 1 summarizes the population's characteristics. Regardless of age and gender, all individuals had a BMI equal to or above $30 \text{ kg}/\text{m}^2$, indicating overweight, with a higher tendency in women. The average waist circumference for the population exceeded 88 cm for women and 102 cm for men, both considered risk factors for cardiovascular diseases. There was no loss of sample, once all patients potentially analyzed were included in the analyzes.

Although women exhibited lower peak handgrip strength on average compared to men, both groups exceeded EWGSOP2 criteria. A similar pattern was observed for skeletal muscle mass, with women having a lower average SMI. The median SMI change concerning EWGSOP2 cutoff points was higher for women. In the Six-Minute Walk Test (6MWT), both women and men achieved values in meters per second greater than the EWGSOP2 criteria.

Physical activity levels were generally high, with women being more active than men. Regarding comorbidities, a significant portion of the population had hypertension (72.1%), dyslipidemia (59.6%), and type 2 diabetes (57.7%). In women, hypertension and metabolic syndrome were more common, while in men, dyslipidemia and diabetes were prevalent.

Table 1: General characterization of the sample of patients with MASLD (n=103).

| Variables: Continuous data | Female | | Male | | p |
|-------------------------------------|--------|-------------------------|------|-------------------------|-------|
| | n | mean±SD or median (IQR) | n | mean±SD or median (IQR) | |
| Age (years) | 76 | 60.01 ± 10.06 | 27 | 61.44 ± 12.18 | 0.587 |
| Height (m) | 76 | 1.88 ± 0.32 | 27 | 2.00 ± 0.00 | 0.002 |
| Weight (Kg) | 76 | 81.46 ± 13.14 | 27 | 88.22 ± 16.81 | 0.066 |
| BMI (Kg/m ²) | 76 | 33.29 ± 5.10 | 27 | 30.46 ± 5.62 | 0.026 |
| Waiste circumference (cm) | 50 | 105.42 ± 11.28 | 14 | 106.50 ± 13.98 | 0.793 |
| Handgrip Strength (Kgf) | 75 | 26.39 ± 6.09 | 27 | 38.11 ± 9.47 | 0.000 |
| Grip strength percentage production | 75 | 83.16 ± 23.11 | 27 | 84.84 ± 22.00 | 0.739 |
| MMI (SMM/height ²) | 49 | 6.66 ± 1.89 | 14 | 9.65 ± 2.32 | 0.000 |
| Delta MMI relative to EWGSOP2 | 49 | 0.34 (-0.66-2.94) | 14 | 2.87 (-0.15-4.25) | 0.024 |
| 6MWT length (m) | 72 | 358.19 ± 80.08 | 27 | 400.67 ± 106.05 | 0.067 |
| 6MWT speed (m/s) | 72 | 0.99 ± 0.22 | 27 | 1.11 ± 0.30 | 0.068 |
| 6MWT percentage production | 72 | 71.84 ± 24.43 | 27 | 78.11 ± 20.03 | 0.193 |
| Categoric data | n | % | n | % | p |
| Sedentary (by IPAQ) | 10 | 17.2% | 6 | 28.6% | 0.268 |
| Physical active (by IPAQ) | 48 | 82.8% | 15 | 71.4% | |
| Systemic arterial hypertension | 57 | 81.4% | 18 | 69.2% | 0.199 |
| Diabetes melittus | 39 | 55.7% | 21 | 84.0% | 0.012 |
| Dislipidemia | 43 | 61.4% | 19 | 79.2% | 0.114 |
| Metabolic syndrome | 28 | 40.6% | 5 | 23.8% | 0.163 |

Note: Categoric data expressed in absolute frequency (n) and relative (%); Continuous data (parametric): mean and standard deviation; Continuous data (non-parametric): median and Interquartile Range (IQR); For gender comparisons: Continuous variables (parametric) were analyzed using the independent samples t-test (p-Student's t-test); Continuous variables (non-parametric) were analyzed using the Mann-Whitney U test; Categorical variables were compared using the Chi-square test (p-Chi-square test). The variables included: SMM (Skeletal Muscle Mass); SMMI (Skeletal Muscle Mass Index); 6MWT (Six-Minute Walk Test).

Table 2 presents the characterization of laboratory tests and insulin resistance and sensitivity markers. Serum concentrations of Aminotransferases (ALT and AST), platelets, and albumin were used to calculate the NAFLD score. For the levels of C-Reactive Protein (CRP), women had a median above the normal reference values, indicating an active inflammatory process, higher than that found in men.

Regarding lipid profile laboratory tests, it was observed that the serum triglyceride results for both genders exceeded the cutoff point (<150 mg/dL) defined by the Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline Update [32]. Only women

had mean total cholesterol levels above the cutoff (<190 mg/dL). Also, high-density lipoprotein (HDL-C) values for women were below the cutoff (≥ 50 mg/dL) defined by the Brazilian Society of Cardiology [33].

Regarding insulin resistance markers, both mean HOMA-IR and the natural logarithm of TyG identified values indicative of insulin resistance. Mean QUICK index values indicated insulin sensitivity in all groups, regardless of nutritional status or diabetes status. In terms of fibrosis classification using the NAFLD score, higher values were observed in men compared to women (Table 2).

Table 2: Laboratory tests and markers of insulin resistance and sensitivity in patients with MASLD.

| Variables: Continuous data | Female | | Male | | p |
|------------------------------|--------|-------------------------|------|-------------------------|-------|
| | n | mean±SD or median (IQR) | n | mean±SD or median (IQR) | |
| ALT (U/L) | 68 | 29.0 (21-36.75) | 26 | 33.5 (23.5-66.25) | 0.122 |
| AST (U/L) | 68 | 26.5 (22-35) | 26 | 33 (26.7-40.25) | 0.024 |
| Albumin (g/L) | 64 | 4.43 ± 0.60 | 25 | 4.34 ± 0.93 | 0.659 |
| Platelets (mm ³) | 68 | 252.4 ± 84.34 | 25 | 215.8 ± 63.57 | 0.029 |
| Creatinine (mg/dL) | 68 | 0.78 ± 0.2 | 26 | 0.91 ± 0.27 | 0.030 |
| C-reactive protein (mg/dL) | 55 | 6.7 (3.31-11.7) | 19 | 2.3 (0.8-4.1) | 0.019 |
| Triglycerides (mg/dL) | 67 | 177.63 ± 78.04 | 22 | 160.86 ± 84.85 | 0.418 |
| Total Cholesterol (mg/dL) | 67 | 194.46 ± 46.47 | 23 | 174.22 ± 38.64 | 0.046 |
| HDL (mg/dL) | 65 | 109.17 ± 42.21 | 21 | 98.95 ± 34 | 0.267 |
| LDL (mg/dL) | 67 | 48.94± 11.71 | 23 | 46.39 ± 10 | 0.319 |
| Glucose (mg/dL) | 65 | 125.01 ± 56.69 | 22 | 142.91 ± 29 | 0.278 |
| Insuline (U/mL) | 50 | 18.44 ± 11.53 | 18 | 19.06 ± 16.43 | 0.884 |
| Homa-IR | 45 | 5.75 ± 4.25 | 18 | 7.87 ± 10.06 | 0.412 |
| TyG | 65 | 9.14 ± 0.68 | 22 | 9.13 ± 0.76 | 0.943 |
| Quick | 50 | 0.48 ± 0.03 | 18 | 0.47 ± 0.04 | 0.266 |
| NAFLD | 67 | -0.77 ± 1.67 | 26 | -0.11 ± 1.21 | 0.040 |

Note: Values expressed as mean and standard deviation; and median and interquartile range; Continuous variables: *p*: Student's T test for independent samples (parametric variables), Mann-Whitney U test for independent samples (non-parametric variables) between genders; Categorical variables: *p*: Chi-square test between genders; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase.

Table 3 describes the variables related to sarcopenia diagnosis following the criteria recommended by EWGSOP2. Regarding the diagnosis of sarcopenia using the algorithm established by EWGSOP2, four individuals showed reduced muscle strength.

Among them, two had decreased Skeletal Muscle Mass (SMM), resulting in a diagnosis of sarcopenia. Out of these two, only one individual exhibited reduced walking speed and was classified with severe sarcopenia.

Table 3: Variables related to the diagnosis of sarcopenia based on the criteria established by EWGSOP2.

| Variables | Female | | Male | | p |
|-------------------------------------|--------|-------|------|-------|-------|
| | n | % | n | % | |
| Handgrip strength | | | | | |
| Below | 1 | 1.3% | 3 | 11.1% | 0.025 |
| Adequated | 74 | 98.7% | 24 | 88.9% | |
| MMI (SMM/height²) | | | | | |
| Below | 23 | 46.9% | 4 | 28.6% | 0.221 |
| Adequated | 26 | 53.1% | 10 | 71.4% | |
| 6MWT | | | | | |
| Below | 7 | 9.7% | 2 | 7.4% | 0.721 |
| Adequated | 65 | 90.3% | 25 | 92.6% | |

Note: Values expressed as absolute (n) and relative frequency (%); *p*: Chi-square test between genders; SMM (Skeletal Muscle Mass); SMMI (Skeletal Muscle Mass Index).

Table 4 outlines the stages of MASLD through liver biopsy and the classification of fibrosis by the NAFLD score. Fifty-nine patients (57.3%) underwent liver biopsy, and 94 (91.3%) had fibrosis classified by the NAFLD score.

It was observed that 35 (62.5%) individuals had mild to moderate steatosis, while 21 (37.5%) had severe steatosis. Mild to moderate steatosis was more prevalent among men (n=11; 68.7%), while severe steatosis was more common among women (n=16;40%). As for the presence of Non-Alcoholic

Steatohepatitis (NASH), 13 individuals (24.08%) had moderate to severe NASH.

Regarding fibrosis classifications, 68 (72.34%) individuals had undetermined or high probability of fibrosis according to the NAFLD score, with a higher prevalence in the male sample.

When assessing fibrosis by liver biopsy, it was observed that 27 (28.72%) and 15 (16.96%) were classified as F1 and F2, and F3 and F4, respectively. Stratification of fibrosis into F3 and F4 was more prevalent among men (n=9;47.4%).

Table 4: Variables related to NAFLD stages by liver biopsy and fibrosis by NAFLD score.

| Variables | Female | | Male | | p |
|--|--------|-------|------|-------|-------|
| | n | % | n | % | |
| Steatosis (By HB) | | | | | |
| Mild and moderate | 24 | 60.0% | 11 | 68.7% | 0.738 |
| High | 16 | 40.0% | 5 | 31.3% | |
| NASH (By HB) | | | | | |
| Absent or mild | 32 | 82.0% | 9 | 60.0% | 0.109 |
| Moderate or high | 7 | 18.0% | 6 | 40.0% | |
| Fibrosis (By HB) | | | | | |
| F0 | 16 | 40.0% | 1 | 5.3% | 0.028 |
| F1 and F2 | 18 | 45.0% | 9 | 47.4% | |
| F3 and F4 | 6 | 15.0% | 9 | 47.4% | |
| Fibrosis (By NAFLD) | | | | | |
| Without or low fibrosis | 23 | 33.8% | 3 | 11.5% | 0.057 |
| In determined or high fibrosis probability | 45 | 66.2% | 23 | 88.5% | |

Note: Values expressed as absolute (n) and relative frequency (%); p: Chi-square distribution between genders; NASH: Non-Alcoholic Steatohepatitis; HB: Hepatic Biopsy

DISCUSSION

Globally, the prevalence of MASLD is on the rise due to increasingly sedentary lifestyles, the globalization of the western diet, and the increasing frequency of obesity, Insulin Resistance (IR), Type 2 Diabetes (T2DM), and dyslipidemia.

As a consequence of the pandemic spread of diabetes and obesity, MASLD is increasingly recognized as the most prevalent chronic liver disease in the world, with an estimated global prevalence of 25%. Although MASLD is highly prevalent on all continents, the highest prevalence has been reported in South America and the Middle East (31%-32%), followed by Asia, the USA, and Europe (23%-27%), and Africa (14%) [34,35]. The current increasing prevalence of MASLD may lead to advanced liver disease and extrahepatic complications. NASH is expected to become the most common indication for liver transplantation in the United States in the near future [36].

As for the presence of comorbidities, our study population showed a high percentage of hypertension (72.1%), dyslipidemia (59.6%), and T2DM (57.7%), with a slightly lower prevalence of metabolic syndrome (31.7%). It was observed that 81.4% of women and 84% of men, respectively, had hypertension. Among men, T2DM was the second most prevalent disease at 79.2%.

It was observed that 62.5% and 37.5% of our sample had mild to moderate and severe steatosis, respectively. Regarding the

presence of NASH, 75.92% had no or mild NASH, while 24.08% had moderate to severe NASH. As for fibrosis classifications, 72.34% of individuals had indeterminate or high probability fibrosis according to the NAFLD score. When assessing the presence of fibrosis through liver biopsy, 28.72% were classified as F1 and F2, while 16.96% were classified as F3 and F4.

Sarcopenia has been associated with an increased incidence and risk of MASLD [37]. MASLD and sarcopenia share important pathogenetic pathways, including Insulin Resistance (IR), chronic systemic inflammation, and vitamin D deficiency, with IR consistently linked to both conditions [38]. The main pathophysiology of sarcopenia is associated with IR, which plays a crucial role in the development of MASLD. The prevalence of sarcopenia is higher in patients affected by MASLD and correlates with the severity of the condition.

In our study, only women had C-Reactive Protein (CRP) levels above the normal reference values, indicating active inflammation. Concerning lipid profile laboratory tests, serum triglyceride results were above the cutoff (<150 mg/dL) defined by the Brazilian Society of Cardiology's 2017 guidelines, with an average of 173.48 mg/dL. Total cholesterol levels were above the threshold (<190 mg/dL) only in women, with an average of 194.46 mg/dL. Women also had High-Density Lipoprotein Cholesterol (HDL-C) values below the cutoff (≥ 50 mg/dL), as

defined by the 2017 Brazilian Society of Cardiology's guidelines, with an average of 48.94 mg/dL.

Regarding glycemic profile analytes and insulin resistance and sensitivity markers, the average fasting glucose levels were above 99 mg/dL, the upper cutoff for euglycemia according to the American Diabetes Association, with an average of 129.54 mg/dL. As for markers of Insulin Resistance (IR), both the mean values of the HOMA-IR index and the logarithm of TyG identified values indicative of insulin resistance. The mean QUICK index values indicated values indicative of insulin sensitivity in all groups, regardless of nutritional status or the presence of diabetes.

Despite the methodological differences used to identify sarcopenia in various studies and considering the specific characteristics of each population, the literature shows a positive association between sarcopenia and MASLD, with a significant prevalence in this population, predominantly in developed countries [39-41].

In a study evaluating 309 MASLD patients, the prevalence of sarcopenia was 8.7% (17.9% in patients with steatosis and 35% in patients with NASH). It has also been shown that there is a linear increase in the prevalence of sarcopenia with the severity of hepatic fibrosis, reaching 20.4% in patients with absent, mild, or moderate fibrosis (F0-F2) and 48.3% in patients with advanced fibrosis or cirrhosis (F3-F4) ($p < 0.001$) (8). However, the diagnostic criteria for sarcopenia in both methods (EWGSOP 1 and 2) have been almost exclusively applied in geriatric populations with other diseases, with no established cutoff points for adult individuals and/or those with MASLD.

Our results showed a very low prevalence ($n=2$) of sarcopenia in MASLD patients, regardless of age and gender, despite having an average BMI of 32.55 kg/m², classified as obese, and an average waist circumference of 105.66 cm, classified as a cardiovascular risk factor. Additionally, the majority of the population was physically active (60.6%), with women being more active (82.8%) compared to men (71.4%). Regarding physical exercise practice, studies suggest that participation in any type of training program appears to positively influence sarcopenia prevalence, as observed by Ferreira et al., in their systematic review of systematic reviews with meta-analysis [42].

Our sample population also had very good results in grip strength, Skeletal Muscle Mass Index (SMI), and functional capacity evaluations, with averages of 29.49 kg/force, 7.32 kg/m², and 1.03 m/s, respectively.

Similar results were observed in the study by Almeida et al., who assessed 57 Brazilian adult individuals from the state of Bahia. The authors found a sarcopenia diagnosis based on EWGSOP1 in only 3.5% of MASLD patients, while the prevalence of probable/pre-sarcopenia was higher based on the EWGSOP2 consensus at 26.3%, compared to 1.8% with EWGSOP [43].

The association between sarcopenia and MASLD still requires further evaluation, considering the standardization and identification of the best diagnostic method for sarcopenia in adult individuals and/or those with MASLD. Since sarcopenia

is often not noticeable in the early stages, detecting probable sarcopenia is essential so that appropriate intervention can be established early [44].

CONCLUSION

In conclusion, the majority of the population was physically active, with women being more active than men. The parameters indicative of sarcopenia had averages above the cutoff points recommended by EWGSOP2, and the prevalence of sarcopenia was very low in patients with MASLD.

The association between sarcopenia and MASLD still requires further evaluation, taking into account the standardization and identification of the best diagnostic method for sarcopenia in adult individuals and/or those with MASLD.

FUNDING

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

CONFLICTS OF INTERESTS

The authors declare not have conflict of any kind.

INSTITUTIONAL REVIEW STATEMENT

The study received approval from the research ethics committee of the University of Health Sciences of Porto Alegre (UFCSPA) and the Irmandade Santa Casa de Misericórdia de Porto Alegre (ISCMPA) under the reference numbers 1.894.929 and 1.856.118, respectively.

Informed Consent Statement: All patients provided informed consent by signing the Informed Consent Form (ICF). All the procedures followed the declaration of Helsinki, and the Brazilian law of protection of personal data (law 13.709/2018).

REFERENCES

1. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *Ann Hepatol.* 2023;29(1):10113.
2. Fernández T, Viñuela M, Vidal C, Barrera F. Lifestyle changes in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis. *PLoS One.* 2022;17(2):e0263931.
3. Araújo AR, Rosso N, Bedogni G, Tiribelli C, Bellentani S. Global epidemiology of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis: What we need in the future. *Liver Int.* 2018;38:47-51.
4. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology.* 2018;67(1):328-357.
5. Panel CP, Berzigotti A, Tsochatzis E, Boursier J, Castera L, Cazzagon N, et al. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis–2021 update. *J Hepatol.* 2021;75(3):659-689.
6. Kim JA, Choi KM. Sarcopenia and fatty liver disease. *Hepatol Int.* 2019;13(6):674-687.

7. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. *Age Ageing*. 2019 Jan 1;48(1):16-31.
8. Petta S, Ciminnisi S, Di Marco V, Cabibi D, Cammà C, Licata A, et al. Sarcopenia is associated with severe liver fibrosis in patients with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther*. 2017;45(4):510-518.
9. Pan X, Han Y, Zou T, Zhu G, Xu K, Zheng J, et al. Sarcopenia contributes to the progression of nonalcoholic fatty liver disease-related fibrosis: A meta-analysis. *Dig Dis*. 2018;36(6):427-436.
10. Yu R, Shi Q, Liu L, Chen L. Relationship of sarcopenia with steatohepatitis and advanced liver fibrosis in non-alcoholic fatty liver disease: A meta-analysis. *BMC Gastroenterol*. 2018;18(1):1-6.
11. Kim G, Kang SH, Kim MY, Baik SK. Prognostic value of sarcopenia in patients with liver cirrhosis: A systematic review and meta-analysis. *PloS one*. 2017;12(10):e0186990.
12. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39(4):412-423.
13. Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*. 2005; 41(6): 1313-21.
14. Poynard T, Munteanu M, Deckmyn O, Ngo Y, Drane F, Castille JM, et al. Validation of liver fibrosis biomarker (FibroTest) for assessing liver fibrosis progression: Proof of concept and first application in a large population. *J Hepatol*. 2012;57(3):541-8.
15. Hart CL, Morrison DS, Batty GD, Mitchell RJ, Davey Smith G. Effect of body mass index and alcohol consumption on liver disease: Analysis of data from two prospective cohort studies. *BMJ*. 2010 Mar 11;340:c1240.
16. Geloneze B, Repetto EM, Geloneze SR, Tambascia MA, Ermetice MN. The threshold value for insulin resistance (HOMA-IR) in an admixed population IR in the Brazilian Metabolic Syndrome Study. *Diabetes Res Clin Pract*. 2006;72(2):219-20.
17. Geloneze B, Vasques AC, Stabe CF, Pareja JC, Rosado LE, Queiroz EC, et al. HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and metabolic syndrome: Brazilian Metabolic Syndrome Study (BRAMS). *Arq Bras Endocrinol Metabol*. 2009;53(2):281-7.
18. Guerrero-Romero F, Villalobos-Molina R, Jiménez-Flores JR, Simental-Mendia LE, Méndez-Cruz R, Murguía-Romero M, et al. Fasting Triglycerides and Glucose Index as a Diagnostic Test for Insulin Resistance in Young Adults. *Arch Med Res*. 2016;47(5): 382-7.
19. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: A simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab*. 2000;85(7):2402-2410.
20. Angulo P, Hui JM, Marchesini G, Bugianesi E, George J, Farrell GC, et al. The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45(4):846-854.
21. Bedossa P. Current histological classification of NAFLD: Strength and limitations. *Hepatol Int*. 2013;7(2):765-770.
22. World Health Organization. Obesity: preventing and managing the global epidemic: Report of a WHO consultation.
23. Lipschitz DA. Screening for nutritional status in the elderly. *Prim Care*. 1994;21(1):55-67.
24. Lean ME, Han TS, Deurenberg P. Predicting body composition by densitometry from simple anthropometric measurements. *Am J Clin Nutr*. 1996;63(1):4-14.
25. IDF. 2023.
26. Marfell-Jones MJ, Stewart AD, De Ridder JH. International standards for anthropometric assessment. 2012.
27. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, et al. A review of the measurement of grip strength in clinical and epidemiological studies: Towards a standardised approach. *Age Ageing*. 2011;40(4):423-429.
28. ATS. ATS statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med*. 2002;166(1):111-117.
29. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Manuel Gómez J, et al. Bioelectrical impedance analysis-part II: Utilization in clinical practice. *Clin Nutr*. 2004;23(6):1430-1453.
30. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. *J Appl Physiol* (1985). 2000;89(2):465-471.
31. Matsudo S, Araújo T, Marsudo V, Andrade D, Andrade E, Braggion G. Questionário internacional de atividade física (IPAQ): Estudo de validade e reprodutibilidade no Brasil. *Rev Bras Ativ Fis Saúde*. 2001:05-18.
32. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care*. 2022;1(45):S17-S38.
33. Faludi AA, Izar MCO, Saraiva JFK. Atualização da Diretriz Brasileira de Dislipidemia e Prevenção de Aterosclerose da Sociedade Brasileira de Cardiologia. *Arquivos Brasileiros de Cardiologia Sociedade Brasileira de Cardiologia* 2017;109(2):1.
34. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: Trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol*. 2018;15(1): 11-20.
35. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;64(1):73-84.
36. Byrne CD, Targher G. NAFLD: A multisystem disease. *J Hepatol*. 2015;62(1):47-64. [Crossref] [Google Scholar] [PubMed]
37. Wijarnprecha K, Panjawanatana P, Thongprayoon C, Jaruvongvanich V, Ungprasert P. Sarcopenia and risk of nonalcoholic fatty liver disease: A meta-analysis. *Saudi J Gastroenterol*. 2018;24(1):12-17.
38. Sinclair M, Gow PJ, Grossmann M, Angus PW. Sarcopenia in cirrhosis-aetiology, implications and potential therapeutic interventions. *Aliment Pharmacol Ther*. 2016;43(7):765-77.
39. Lee YH, Kim SU, Song K, Park JY, Kim DY, Ahn SH, et al. Sarcopenia is associated with significant liver fibrosis independently of obesity and insulin resistance in nonalcoholic fatty liver disease: Nationwide surveys (KNHANES 2008-2011). *Hepatology*. 2016;63(3):776-86.
40. Wang YM, Zhu KF, Zhou WJ, Zhang Q, Deng DF, Yang YC, et al. Sarcopenia is associated with the presence of nonalcoholic fatty liver disease in Zhejiang Province, China: a cross-sectional observational study. *BMC Geriatr*. 2021;21(1):55.
41. Moon JH, Koo BK, Kim W. Non-alcoholic fatty liver disease and sarcopenia additively increase mortality: A Korean nationwide survey. *J Cachexia Sarcopenia Muscle*. 2021;12(4):964-72.
42. Ferreira LF, Scariot EL, da Rosa LHT. The effect of different exercise programs on sarcopenia criteria in older people: A systematic review of systematic reviews with meta-analysis. *Archives of Gerontology and Geriatrics*. 2023;105:104868.
43. Almeida NS, Rocha R, de Souza CA, da Cruz ACS, Ribeiro BDR, Vieira LV, et al. Prevalence of sarcopenia using different methods in patients with non-alcoholic fatty liver disease. *World J Hepatol*. 2022;14(8):1643-51.

44. Arnal-Gómez A, Cebrià IIMA, Tomas JM, Tortosa-Chuliá MA, Balasch-Bernat M, Sentandreu-Mañó T, et al. Using the Updated

EWGSOP2 Definition in Diagnosing Sarcopenia in Spanish Older Adults: Clinical Approach. J Clin Med. 2021;10(5):1018.