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Short Communication

Evaluating Sarcopenia in Liver Disease: Assessment of Skeletal Muscle Mass by Computed Tomography is not Related to MASLD by Liver Biopsy

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ABSTRACT

Background: The relationship between sarcopenia and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has been widely studied. However, there are still a lack in the knowledge about the best tools to asses sarcopenia in MASLD patients, and what cut-off points for the diagnosis criteria for sarcopenia are suitable for this population.

Objective: To compare the Skeletal Muscle Mass (SMM) assessed by Computed Tomography (CT) in patients with MASLD assessed by Liver Biopsy (LB). Methods: Cross-sectional study with patients attended at the outpatient clinic in a tertiary hospital of southern Brazil. Were included individual aged >18 years, with MASLD confirmed by LB. The SMM was assessed by the quantification of the transverse area of the third lumbar vertebra (L3) in the CT. The results were analyzed using the test Anova one-way.

Results: 66 patients were included, and analyzed in groups by the level of fibrosis by LB. The mean age was 58.75 years, and most were women (77%; n=51). There was significant difference in diabetes, weight, abdominal circumference, AST levels, bilirubin, LDL cholesterol, all increasing according the level of fibrosis. The SMM were also higher, according to the level of fibrosis, being 46.61+7.28 cm^2/m^2 in F0; 46.30+6.8 in F1; 45.34+11.09 in F2; 55.08+15.97 in F3 and; 50.2+9.09 in F4, although without a difference statistically significant (p=0.172).

Discussion: The CT assess only a transverse area of one muscle, and it has been debated if it represents well the whole-body SMM. Also, the CT is evaluator-dependent, which can lead to analyzing bias.

Conclusion: For this sample, the SMM assessment by CT do not showed difference, and the SMM increasing with worst fibrosis diagnosis go against the state-of-the-art in sarcopenia assessment. Further studies are necessary comparing SMM assessment specifically for liver patients.

Keywords: Sarcopenia; MASLD; Fibrosis; Tomography; NAFLD

INTRODUCTION

The relation between Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and sarcopenia have been widely studied in the recent years [1]. They apparently share some physiological pathways, making possible to find a connection in the etiology for both conditions, such as the insulin resistance, the loss of skeletal muscle mass, and the fat accumulation in other tissues, as muscle and hepatocytes [2,3].

Although some consensuses to diagnose sarcopenia have emerged in the last years, the mostly of them are for older

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people, and not for patients of other conditions, such MASLD [4,5]. So, the main authors in the field are still conducting researches to find ways to diagnose sarcopenia in MASLD patients, that can relate with this specific condition, even trying to define the most appropriate cutoff points for this condition [6,7].

The objective of this study was to compare the results of Skeletal Muscle Mass (SMM) assessment by Computed Tomography (CT) with the MASLD degree evaluated by Liver Biopsy (LB).

MATERIALS AND METHODS

Observational and prospective study, conducted according the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines [8]. Patients aged >18 years, diagnosed with MASLD by LB, treated on the Gastroenterology and Hepatology outpatient clinic at Irmandade Santa Casa de Misericordia de Porto Alegre (ISCMPA), a tertiary care hospital in southern Brazil, between 2017 and 2020, were included.

Were excluded patients with hepatitis B or hepatitis C virus; with significant alcohol consumption (>20 g/day for women and >30 g/day for men); with other causes of chronic liver disease; secondary causes of MASLD and; patients with Hepatocellular Carcinoma (HCC) [9]

Liver biopsy was indicated according to the guideline of the American Association for Study of Liver Disease. LB were analyzed by a professional with experience in liver pathology blinded for patient's data, using the NAFLD Activity Score for histopathological analysis [10]. MASLD was defined according the new classification.

CT was performed to assess muscle mass, by analyzing the transverse area of the third lumbar vertebra (L3), using specific software [11]. For this quantification, L3 was identified, and the transverse area of the abdominal and paravertebral wall muscles involved at the height of L3 was measured. The value obtained in square centimeters was divided by the patient's height (in meters) squared, resulting in the Skeletal Muscle Mass Index (SMI).

Other indicators were also assessed, such as weight and height (calculating the body mass index by dividing weight by height square); clinical conditions, such as Systemic Arterial Hypertension (SAH), type 2 Diabetes Mellitus (DM2), and dyslipidemia; and blood tests as Total Cholesterol (TC), Low-Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL) cholesterol, Triglycerides (TG), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), total and direct bilirubin, prothrombin time, albumin, platelets, glucose, insulin, C-Reactive Protein (CRP) and ferritin. In addition, resistance to insulin action was estimated through Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) [12].

The Kolmogorov-Smirnov test was used to assess the normality. To compare continuous variables between groups, Independent sample Student's T-Test was used. The analyzes were processed in the Statistical Package for the Social Sciences program (PASW Statistics for Windows, version 18.0. Chicago: SPSS Inc). The level of significance assumed was 5% and the Confidence Interval (CI) was 95%. The data were analyzed grouping the patients into two different groups: G1 being the patients with less liver impairment (F0, F1 and F2); and G2 the patients with advanced fibrosis (F3) and cirrhosis (F4).

The project was approved by the Research Ethics Committee of the Federal University of Health Sciences of Porto Alegre, under letter n° 57328416.8.0000.5335. Volunteers read and signed the Informed Consent Form. The entire research was conducted following Resolution 196/96 of the National Health Council (Brazil) and adhered to the principles of the Declaration of Helsinki for research involving human subjects. Data were processed in accordance with the General Data Protection Law (Brazilian Law n° 13.709/2018).

RESULTS

The final sample consisted of 66 patients, being mostly women, as can be seen in Table 1. The sample characterization data, such as age, gender and BMI did not showed statistically significant difference. However, some discriminant data were different between the groups, being weight, height, abdominal circumference, AST, bilirubin, insulin and HOMA-IR means significantly higher in G2, as well the prevalence of DM were higher in this group; while total and LDL cholesterol, and platelets were significantly higher in G1.

About the SMM, the mean was statistically higher in G2 than in G1. When divided by stages, is possible to see that the means are below the total mean for stages F0, F1 and F2 (46.62 ± 7.29; 46.31 ± 6.8; 45.34 ± 11.1 cm^2/m^2, respectively), while F3 and F4 are above it (55.08 ± 15.98; 50.209.1 cm^2/m^2, respectively).

Table 1: Sample Characteristics categorized by MASLD levels (n=66).

Variable*	Group 1 (n=34)	Group 2 (n=32)	Total (n=66)	p
SMM (cm^2/m^2)	46.28 ± 7.63	51.42 ± 11.12	48.77 ± 9.76	.031
Age (Years)	58.18 ± 9.28	59.38 ± 12.28	58.76 ± 10.77	.655
Weight (Kg)	79.79 ± 12.64	89.4 ± 19.04	84.45 ± 16.66	.018[1]

Height (m)	1.57 ± 0.06	1.62 ± 0.09	1.59 ± 0.08	.010[1]
BMI	32.31 ± 5.11	34 ± 6.84	33.13 ± 6.03	.259
ALT	32.71 ± 18.45	43.03 ± 35.64	37.71 ± 28.38	.141
AST	28.32 ± 10.28	46.69 ± 29.76	37.23 ± 23.7	.0011
Bilirubin	0.55 ± 0.33	1.18 ± 1.04	0.86 ± 0.82	.002[1]
Albumin	4.45 ± 0.81	4.25 ± 0.44	4.35 ± 0.66	.241
Total chol	207.79 ± 46.74	173.32 ± 51.85	191.35 ± 51.84	.006[1]
HDL chol	51.47 ± 14.1	48.23 ± 10.87	49.92 ± 12.67	.306
LDL chol	125.15 ± 41.55	85.04 ± 35.02	108.68 ± 43.49	.000[1]
Triglycerides	164.24 ± 55.14	179.93 ± 115.88	171.71 ± 88.96	.489
Glucose	106.82 ± 33.83	124.81 ± 46.74	115.53 ± 41.27	.081
Insulin	15.11 ± 8.92	21.78 ± 21.22	18.06 ± 10.9	.045[1]
HOMA-IR	4.34 ± 3.08	6.72 ± 3.41	5.36 ± 3.4	.023[1]
CRP	6.45 ± 5.94	8.58 ± 10.11	7.38 ± 7.99	.378
Creatinine	0.79 ± 0.2	0.81 ± 0.26	0.8 ± 0.23	.749
Ferritin	172.93 ± 145.11	258.24 ± 337.86	212.43 ± 254.28	.222
Hemoglobin	13.56 ± 1.34	13.47 ± 2.24	13.51 ± 1.82	.837
Platelets	263.34 ± 76.02	174.97 ± 69.97	219.86 ± 85.1	.000[1]
Gender: Female	29 (85.29)	22 (68.75)	15 (22.72)	.112
SAH	24 (70.58)	26 (81.25)	50 (75.75)	.320
DM	15 (44.11)	24 (75)	39 (59.09)	.010[1]
Dyslipidemia	12 (35.29)	21 (65.62)	37 (56.06)	.133
MS	11 (32.35)	23 (71.87)	38 (57.58)	.310

Note: *Continuous data presented in mean+SD; Categoric data presented in n (%); SD: standard deviation; n: total sample; %: relative sample; p: Student's T test to independent samples; [1] difference statistically significant; Kg: Kilogram; m: meters; BMI: Body Mass Index; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; Chol: Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; CRP: C-Reactive Protein; SMM: Skeletal Muscle Mass; cm^2/m^2: Centimetre Square by Meter Square; SAH: Systemic Arterial Hypertension; DM: Diabetes Mellitus; MS: Metabolic Syndrome.

DISCUSSION

In this study, although there was a statistically significant difference in Skeletal Muscle Mass (SMM) between G1 and G2, the indices were higher in G2, precisely in those patients with greater hepatic impairment, in the opposite way to that would be expected. Most studies correlating hepatic diseases such as MASLD, fibrosis, and cirrhosis with sarcopenia have reported that muscle mass tends to decrease as liver impairment increases (an inverse correlation) [13,14]. This phenomenon is attributed to the shared physiological pathways between the two conditions. For instance, insulin resistance, closely linked to the onset of hepatic diseases, is also considered a risk factor for sarcopenia.

Apart from the shared physiological pathways, a direct relationship between sarcopenia and MASLD exists, who found that myostatin activation in SMM may be influenced by hepatic malfunction caused by fat accumulation in hepatocytes [15,16].

Additionally, various authors suggest that hepatic diseases decrease the macronutrient absorption rate, influencing protein synthesis in SMM and directly reducing the resynthesize phenomenon, as hepatocytes gradually lose the capacity for synthesis [17,18].

As reported, the reduction in SMM, beyond merely explaining hepatic impairment progression, may activate stellate cells with fibrogenic properties in the liver, thereby increasing the risk of fibrosis, cirrhosis, and hepatocellular carcinoma [19]. Thus, not only can low SMM levels explain advanced hepatic impairment, but greater hepatic impairment can also elucidate SMM reduction.

Considering the literature's solid evidence on the liver disease-sarcopenia relationship, it can be hypothesized that the discrepant result in this sample may be attributed not directly to the sample itself, but rather to the method of assessment employed for SMM quantification.

Although Computed Tomography (CT) is recommended for muscle mass evaluation by most sarcopenia consensuses, being a cheaper test than other options and offering lower radiation levels compared to Dual-Energy X-ray Absorptiometry (DXA) and Magnetic Resonance Imaging (MRI), CT has been discussed for its inherent errors [20].

Firstly, despite a correlation between SMM evaluation by DXA (the gold standard) and CT for elderly patients, this relationship has not been fully explored in patients with other pathologies that may directly affect specific muscle groups or alter the proportion of other body components, such as fluid accumulation (ascites, a common manifestation of hepatic diseases) and intramuscular lipid accumulation (also common in hepatic steatosis) [21].

In these cases, evidence points toward bio-impedance analysis and DXA as more suitable examinations, as they can detect the accumulation of other components in SMM and assess the entire body, unlike CT, which examines only a slice of muscle, generally assessed at the level of the third lumbar vertebra) [22].

CT may also face issues related to equipment calibration and evaluator analysis. Regarding equipment calibration, the assumption that the equipment returns a value of zero for water, expected for a well-calibrated scanner, can be misleading, increasing the risks of precision errors in muscle density determination [23]. Regarding the evaluator, it's important to note that, unlike DXA and Bioelectrical Impedance Analysis (BIA), CT-based SMM assessment is evaluator-dependent, as a professional need to delineate the contours of the muscle being evaluated. Thus, not only there is a possibility of evaluator bias, but the image quality, with shadows or undefined lines, can influence the final assessment result [24].

CONCLUSION

In conclusion, for this sample, a higher level of hepatic impairment is related with higher amount of SMM level assessed by CT, although there may be a strong influence of the assessment method on the presented results.

The major limitation of this study is that the evaluation of SMM by CT, as reported, may not be the best choice for assessing SMM in sarcopenic hepatic patients due to its significant margin of error and inherent biases in this assessment model. Furthermore, it is recommended that new studies with larger samples be conducted, comparing different methods of SMM evaluation in hepatic patients to validate methods and increase the security and efficacy of collected data.

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CONFLICTS OF INTERESTS

The authors declare not have conflict of interest of any kind for the realization of this study.

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