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# Association between sarcopenia and diabetes in community dwelling elderly in the Amazon region – Viver Mais Project

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ABSTRACT

*Background:* Studies indicate the intrinsic relationship between sarcopenia and diabetes mellitus (DM) pathophysiological mechanisms. Changes in insulin and muscular metabolism are features of diabetic patients and can interact as sarcopenic accelerators. Conversely, sarcopenic patients feature lower glucose tolerance and higher serum insulin levels, predisposing them to DM.

*Objective:* To study the association between sarcopenia and DM in a community-dwelling elderly population of the Amazon region.

*Methods:* Cross-sectional study, performed in Belém, Brazil, with 1078 patients aged above 60 years old from the Viver Mais Project (VMP). The definition of sarcopenia was based in the European Working Group on Sarcopenia in Older People (EWGSOP). Calf circumference > 31 cm was considered normal, muscle strength was discriminated by BMI and measured with the hand grip test, and gait speed < 0.8 m/s configured low performance. DM was diagnosed when reported by the patient or medical form, use of hypoglycemic medications/insulin and in the presence of fasting glucose > 126 mg/dl or glycated hemoglobin (HbA1c) > 6.5% on two occasions. Other medical and socio-demographic data were extracted from medical forms.

*Results:* The frequency of sarcopenia was 9.4%, while DM was present in 36.87% of the patients, and had an increased occurrence in the sarcopenic group. Female sex, advanced age, DM, coronary insufficiency, osteoporosis, body mass index, waist circumference, triglycerides and functionality were associated with sarcopenia. In multivariate analysis, sarcopenia remained strongly associated with DM (OR: 3.208, 95%CI: 1.784–5.769).

*Conclusion:* This study describes strong and independent association between sarcopenia and DM. To further clarify these findings, broader prospective cohorts are necessary.

## 1. Introduction

Sarcopenia represents a true geriatric syndrome characterized by gradual and widespread loss of muscle mass associated with decline of muscular function, implying great compromise of the functionality of the elderly, lower quality of life and premature death (Cruz-Jentoft et al., 2010; Shaw et al., 2017).

Due to its high prevalence in the elderly, many studies have verified the association of sarcopenia with other chronic diseases, such as Diabetes Mellitus (Landi et al., 2013; Morley et al., 2014; Nomura et al., 2018).

Several studies have shown that both can share etiological pathways, including reduced physical activity, insulin resistance, chronic inflammation and mitochondrial dysfunction, as well as common characteristics such as mobility limitation and independence (Landi et al., 2013; Trierweiler et al., 2018).

Sarcopenia leads to the lower uptake of muscle glucose and hyperglycemia (Nomura et al., 2018; Santilli et al., 2014; Umegaki, 2015). DM predisposes changes in different body tissues, which can induce sarcopenia, regardless of age, setting up a direct relationship between the two entities in which DM could have causal precedence (Abdelhafiz and Sinclair, 2015; Cetrone et al., 2014).

Systematic review and meta-analysis have shown that people with diabetes have an increased risk of 50–80% for physical disability (Wong

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et al., 2013). Adults with DM have shown lower limb muscle mass and functional capacity compared to adults without diabetes (Wang et al., 2016).

Thus, knowing the possible relationship between sarcopenia and DM is fundamental, since the pathophysiology interacts and can create a vicious cycle, requiring challenging medical treatment. The aim of this study is to contribute to data on the association between sarcopenia and DM, reporting the findings of a community dwelling elderly population in the Amazon region.

## 2. Materials and methods

### 2.1. Research and design of the study population

This is a cross-sectional study, with participants of the Viver Mais Project (VMP) of Hospital Cynthia Charone (HCC), in Belém, Pará, Brazil. The VMP is a prospective study that began in April 2017 and is still in progress. The project includes people with spontaneous demand for geriatric services, in addition to cognitive and physical activities, with focus on prevention or rehabilitation.

Elderly people aged 60 years or more, of both sexes, who were able to ambulate and perform the handgrip test, were included. The first protocol evaluation was performed between April 2017 and April 2018. Individuals under the age of 60 years, those with incomplete data and those who did not agree to participate in the study were not included.

Participants responded to the Multidimensional Evaluation of Elderly (MEE), structured questionnaire, divided into 5 sections (clinical, functional, cognitive, physical, nutritional and psychological/social), implemented by multidisciplinary-trained team (doctor, nutritionist, physiotherapist, occupational therapist and psychologist), covering various aspects, such as personal data, current and previous illnesses, medications, nutritional parameters, functionality, mobility, falls, cognitive assessment and social economic support. Nutritionists performed anthropometric measurements and functional tests were applied for physical therapists. After the first protocol evaluation, laboratory tests were requested, with samples collected through peripheral venous puncture after fasting for 12 h.

Thirteen hundred (1300) elderly were evaluated in the above-mentioned period; however, only 1078 patients fulfilled the inclusion criteria. In total, 222 patients were excluded due to incomplete information or because they were aged below 60 years. Of the 1078, sarcopenia was diagnosed in 101 patients, 39 fulfilled the criteria for severe sarcopenia and the remaining 65 seniors were classified with pre-sarcopenia (Fig. 1).

### 2.2. Measurements

The analyzed variables were: demographic data, smoking, alcoholism, performance in basic and instrumental activities of daily life, comorbidities, body mass index (BMI), waist circumference (WC), calf circumference (CC), handgrip, gait speed and the results of laboratory tests: total cholesterol (TC), high-density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, creatinine, fasting glucose and glycated hemoglobin (HbA1c).

Sarcopenia was defined according to the European Consensus, published in 2010 by EWGSOP (Cruz-Jentoft et al., 2010), as the progressive decline in skeletal muscle mass, associated with decreased muscle strength and/or worsening physical performance. According to the same authors, pre-sarcopenia consists only of the loss of skeletal muscle mass, while severe sarcopenia is present when the three criteria are included.

Muscle mass was evaluated by measuring the circumference of the left calf, in the most prominent region, with the help of an elastic tape measure. Values smaller than 31 cm were considered lower than normal (Cruz-Jentoft et al., 2010). Decreased handgrip was estimated with a manual digital dynamometer in kg (branded Electronic Hand Dynamometer Constat R model 14192-709E). Three measures were carried out in each arm, considering the best result. The cutting point was adjusted according to sex and BMI (Cruz-Jentoft et al., 2010). Gait speed was measured by the timing of the time, in seconds, while the patient was travelling a distance of 4 m at their usual speed. When the participants achieved a speed of less than 0.8 m/s, they were defined as low performance (Cruz-Jentoft et al., 2010).

The diagnosis of DM was confirmed by treatment with oral hypoglycemics or insulin or by laboratory findings of fasting glucose $\geq$126 mg/dl or HbA1c $\geq$6.5% on two occasions (Sociedade Brasileira de Diabetes, 2017).

The patient was considered as having a certain disease, if confirmed in a medical report or medical record, besides the use of medication for the reported disease.

### 2.3. Statistical analysis

The characteristics of the sample were expressed through average, median, variance, and percentage. The comparison between two groups with non-parametric continuous numeric variables was carried out by Mann-Whitney test. For comparison between more than two nonparametric continuous variables Kruskal Wallis test was used. The Chi Square test was used for comparison of categorical variables.

Factors significantly associated with sarcopenia in univariate analysis ($p < 0.005$) were included in multivariate analysis, using binary

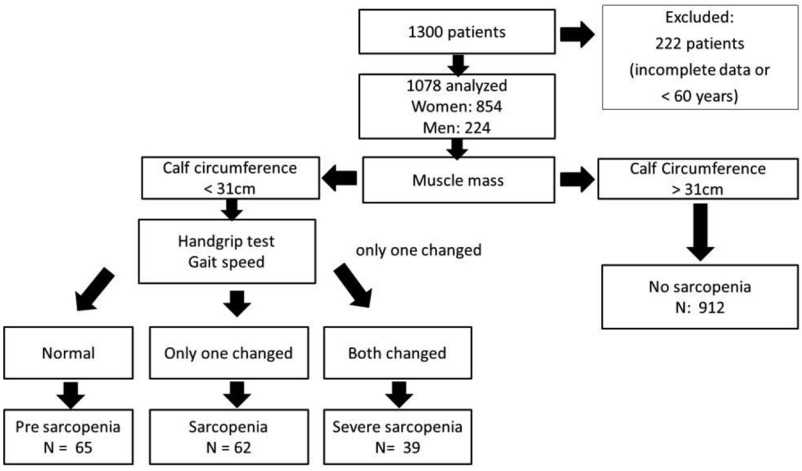


**Fig. 1.** Flow chart of study participants.

logistic regression strategy to identify the appropriate sets of covariates associated with sarcopenia, which maintained a statistically significant relationship. The values of the Odds Ratio (OR) with 95% confidence intervals (95%CI) were also presented.

For all statistical tests, the level of statistical significance used was 5%, with tests with a descriptive level (p) less than 0.05 being statistically significant. The data were structured in Microsoft Office Excel 2010 in conjunction with the Software Epi Info 7.1 and analyzed through the Statistical Package for the Social Sciences (SPSS) software, version 17.0.

### 2.4. Ethical aspects

This study was approved by the Research Ethics Committee of the University of the State of Pará (UEPA), under opinion No. 2.429.987 and according to the Helsinki declaration. Individuals were consulted, had the survey explained and agreed to participate by signing the informed consent form.

## 3. Results

A thousand and seventy eight (1078) elderly individuals were included, with 79.2% being female. The frequency of sarcopenia and DM was 9.4% and 36.8%, respectively. Socio-demographic and clinical characteristics are described in Table 1.

Characteristics significantly associated with sarcopenia were female sex, age, DM, coronary insufficiency, osteoporosis, BMI, WC, triglycerides and performance in basic activities of daily living (BADLs), by the Katz scale and instrumental activities of daily living (IADLs), by the Lawton scale.

Table 2 presents the percentage of diagnosis of DM and the absolute values of fasting blood glucose and glycated hemoglobin, distributed by the profile of sarcopenia.

Table 3 presents the multivariate analysis with corrected OR and confidence interval of statistically significant variables with outcome of sarcopenia and that could skew the relationship initially found with the frequency of DM. Relevant association was observed between the two diseases in sarcopenic elderly of the Amazon region (OR: 3.208, 95% CI 1.784–5.769, $p < 0.0005$) when compared to the non-sarcopenic group.

**Table 1**
Socio-demographic and clinical characteristics of patients and with and without sarcopenia participating in the study.
Source: Own elaboration.

| Variables | Non sarcopenic N = 977 (90.6%) | Sarcopenic N = 101 (9.4%) | P |
|---|---|---|---|
| Sex | | | |
| Female (%) | 764 (78.2) | 90 (89.1) | 0.005 |
| Age (median in years) | 69 (60–99) | 79 (60–103) | 0.0005 |
| Schooling (median in years) | 11 (0–18) | 6 (0–17) | 0.0005 |
| Marital status (%) * | | | < 0.0005 |
| Single | 152 (15.7) | 15 (14.9) | |
| Married | 451 (46.6) | 32 (31.7) | |
| Divorced | 95 (9.9) | 5 (4.9) | |
| Widower | 269 (27.8) | 49 (48.5) | |
| Life habits (%) | | | |
| Alcoholism | 145 (17.5) | 10 (11.5) | 5.303 |
| Smoking | 176 (20.9) | 16 (18.1) | 0.334 |
| Katz scale (%) * | | | < 0.0005 |
| Independent | 938 (98.3) | 86 (86.0) | |
| Partial dependent | 9 (1.0) | 5 (5.0) | |
| Total dependent | 7 (0.7) | 9 (9.0) | |
| Scale of Lawton (%) * | | | < 0.0005 |
| Independent | 804 (84.3) | 42 (42.0) | |
| Partial dependent | 140 (14.7) | 51 (51.0) | |
| Total dependent | 10 (1.0) | 7 (7.0) | |
| Comorbidities (%) | | | |
| Diabetes Mellitus | 210 (22.8) | 35 (36.8) | 0.002 |
| Coronary insufficiency | 23 (2.5) | 7 (7.4) | 0.016 |
| Stroke | 27 (2.9) | 7 (7.4) | 0.032 |
| COPD | 20 (2.2) | 6 (6.4) | 0.028 |
| Depression | 75 (8.2) | 14 (14.7) | 0.031 |
| Dementia | 29 (3.0) | 17 (16.8) | < 0.0005 |
| Osteoporosis | 241 (26.2) | 38.0 (40.0) | 0.004 |
| Anthropometric measurements BMI | | | |
| (Kg/2height) (median) | 28.7 | 23.5 | < 0.0005 |
| Waist circumference (cm) | (18.3–41.6) | (16.4–33.9) | < 0.0005 |
| (median) | 100 (76–132) | 90 (79–107) | |
| Laboratory tests (median) | | | |
| Total cholesterol | 192.0 | 196.0 | 0.832 |
| HDL | (107–312) | (131–256) | 0.219 |
| LDL | 50.0 (30–102) | 52.0 (31–80) | 0.242 |
| Triglycerides | 105.0 (22–218) | 108.0 (47–156) | 0.040 |
| Creatinine | 150.0 (60–610) | 129.0 (59–391) | 0.860 |
| HbA1c | 0.7 (0–7) | 0.6 (1–96) | 0.585 |
| | 6.1 (4.7–11.2) | 6.6 (8.4–5.3) | |
| Fasting blood glucose | 100.0 (71–233) | 105.0 (78–240) | 0.460 |

$p < 0.05$.
Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; HbA1c, Glycated Hemoglobin HbA1c.
* Missing data by the absence in the chart.

## 4. Discussion

The frequency of sarcopenia in the studied population was 9.4%, a result which is consistent with the findings of other authors in non-institutionalized elderly (Hai et al., 2017; Sun et al., 2017). According to EWGSOP, the frequency of sarcopenia ranges from 5 to 13% in the elderly aged 60–70 years, increasing to 11–50% for those over 80 years (Cruz-Jentoft et al., 2010). So far, there have been no other studies in the Amazon region of Brazil.

The main finding of this study was identifying the relationship between sarcopenia and DM in a population of community-dwelling elderly in a city in the North of Brazil, independent of other variables possibly associated with the metabolic disorder.

It was observed that the frequency of DM was higher in sarcopenic subjects (OR = 3.208, IC 95%) when compared to the non-sarcopenic after adjustment for age, gender, comorbidities, functionality and anthropometric variables.

This finding is consistent with most of the literature, such as the study by (Wang et al. (2019)), which included more than 1000 elderly residents in China and concluded that the elderly with DM have a higher frequency of sarcopenia when compared to non-diabetics, and that the risk is 1.56 times greater.

A case-control study in Korea (Kim et al., 2014) found an independent relationship between low muscle mass (defined by skeletal muscle mass/height$^2$) and diabetes. For them, the risk of low muscle mass was approximately two- to four-times greater in elderly people with type 2 diabetes, even after adjusting for confounding factors. Studies by Leenders et al. Lenders et al. (2013) and Morley et al. (2014) found that elderly patients with type 2 DM had a rapid decline in lean lower limb mass, muscle strength and functional capacity when compared to the normoglycemic control group.

The DM would act as precipitating factor of changes such as loss of strength and functional capacity, in addition to several limitations, the predisposing clinical picture of physical inactivity, immobility, weakness and, in some cases, malnutrition (Landi et al., 2013; Volpato et al., 2012). These factors, individually or combined, predispose to accelerated loss of muscle mass featured in sarcopenic individuals, expressed in the poorer performance in physical tests and smaller anthropometric values, and may even indicate a worst prognosis (Kim

**Table 2**
Diagnosis of diabetes and glycated hemoglobin values and fasting glucose according to the classification of sarcopenia.
Source: Own elaboration.

| Clinical parameters | Non sarcopenic N = 912 (84.6) | Pre sarcopenic N = 65 (6.0) | sarcopenic N = 62 (5.8) | Severe sarcopenia N = 39 (3.6) | P |
|---|---|---|---|---|---|
| Diagnosis of DM (%) HbA1c (median) | 199 (23.0) | 11 (19.0) | 16 (31.4) | 16 (41.0) | 0.029 |
| | 6.4 (5.0-9.3) | 5.8 (5.7–6.5) | 7.9 (6.9–9.1) | 5.5 (5.4–5.7) | 0.683 |
| Fasting glucose (median) | 106 (87-173) | 98 (87–135) | 116 (105–138) | 94.5 (87–102) | 0.658 |

$P < 0.05$.
Abbreviations: DM, diabetes mellitus; Glycated hemoglobin HbA1c.

**Table 3**
Multivariate analysis of risk factors associated with sarcopenia.
Source: Own elaboration.

| Variables | OR | IC (95%) | P |
|---|---|---|---|
| Female Sex | 0.353 | 0.152–0.816 | 0.015 |
| Age | 1119 | 1.160–1.077 | < 0.0005 |
| BMI | 0.686 | 0.973–0.484 | 0.035 |
| Abdominal circumference | 0.908 | 0.880–0.936 | < 0.0005 |
| Katz | 1.549 | 3.792–0.633 | 0.338 |
| Lawton | 1.948 | 1.056–3.591 | 0.033 |
| Diabetes Mellitus | 3.208 | 1.784–5.769 | < 0.0005 |
| Coronary insufficiency | 2.817 | 8.330–0.953 | 0.061 |
| Stroke | 1.276 | 0.389–4.193 | 0.688 |
| COPD | 0.993 | 3.493–0.282 | 0.991 |
| Depression | 1.817 | 0.793–4.165 | 0.158 |
| Dementia | 1.868 | 5.404–0.646 | 0.249 |

$P < 0.05$.
Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; OR, Odds Ratio; IC, 95% confidence interval.

et al., 2014; Umegaki, 2015).

Overall, to date there are still multiple pathways from which to explain the relationship between sarcopenia and DM. The main theories focus in the inflammatory state, insulin resistance and depression/anxiety.

The inflammatory status theory is based on the relationship between the hyperglycemia mediated by DM and the activation of catabolic agents. These would be responsible for the decrease in anabolic substances, such as testosterone, GH, and insulin, while being the main pathway to chronic immune-mediated damage to body tissues, particularly skeletal mass (Katta et al., 2010).

The consequent reduction of muscle mass would cause a cascade of metabolic and physical changes that would result in progressive predisposition to sarcopenia, as well as reinforcing the cycle of hyperglycemia and inflammatory chronic systemic state (Nomura et al., 2018; Santilli et al., 2014; Umegaki, 2015).

However, in this study there was no significance between glucose levels and the diagnosis of sarcopenia. The current literature disagrees about the significance of this finding; while some authors state that the relationship is unlikely or inconsequential in the short-term, others cite it as vital to the bridge between DM and sarcopenia, as stated by the inflammatory status theory. Our finding corroborates the first scenario, but it is worth mentioning that time of diagnosis and treatment was not evaluated in our analysis, which can adversely affect the interpretation of the data when bearing in mind patients with long-term glycemic control who recently developed sarcopenia. A better clarification of this specific relationship is possible through longitudinal studies aimed at this population after the diagnosis of disease, or even before that, as some studies indicate that most of the muscle loss induced by hyperglycemia occurs in the early stages of disease, when it is rarely diagnosed or treated correctly (Kalyani et al., 2015; Lien et al., 2018).

The theory of insulin resistance characterizes the muscle mass and insulin absorption capacity as the main agents of vicious progression between DM and sarcopenia.

Insulin resistance triggered by chronic metabolic changes such as dyslipidemia, obesity, high blood pressure and DM induce less muscle glucose supply, causing a reduction of lean body mass, which in return led to greater systemic insulin resistance, thus making the cycle vicious (Cleasby et al., 2016).

Similarly, in sarcopenia started by other causes, loss of muscle mass would eventually evolve with insulin resistance, and possibly DM, again completing the cycle.

The theory of anxiety/depression focuses on the relationship between physical exercise, the presence of fatigue, nutritional/eating habits and the loss of muscle mass.

An increasingly prevalent and notorious disease, when diagnosed, DM is able to change the everyday life of the individual, and the reaction to these variable changes according to the context of the patient.

The use of multiple medications, the need for insulin therapy, concern about complications, and long-term treatment obligation associated with important glycemic variability is able to profoundly affect the individual's emotions (Lien et al., 2018).

The presence of manifestations of depression and anxiety, especially in patients of advanced age, are capable of harming the therapeutic management, as well as preventing the practice of healthy life habits, in particular exercise. As a result, the development of sarcopenia would be inevitable, and the control of blood sugar difficult. This path would be even more severe and important in patients who already present a predisposition to emotional disorders or who have low levels of education (Jang, 2016; Lien et al., 2018).

In this study, when assessed in univariate analysis there was a significant association between sarcopenia and depression; however, this proved to only be a confusion factor, as the association was lost in multivariate analysis, demonstrating that, at least in this population, this pathway was not prevalent.

Other factors that were statistically correlated with sarcopenia were included in the multivariate analysis shown in Table 3. This is the first study of this area that includes not only significant samples but also a more thorough assessment of the data. Among the variables that showed significance was the female gender as a factor of protection, while other variables lost such significance, for example depression, dementia and COPD, reinforcing the hypothesis that the depression and anxiety pathway was not present in this specific population, and stressing the importance of multivariate analysis for the identification of these confounding factors.

The relationship between the two diseases has been widely researched, but the main active mechanism remains unclear. Studies emphasize the existence of feedback that accelerates the progression of both, and should always be searched together (Morley et al., 2014).

This study has some limitations. It is a cross-sectional study, which restricts the ability to prove causality between events, allowing only correlations to be inferred. The frequency of sarcopenia in the studied population may have been underestimated due to the non-availability of the gold standard exam for muscle mass assessment – total body densitometry (DEXA), which resulted in the non-identification of obese sarcopenia. Instead, the present study used calf circumference, regarded as the most sensitive indicator of muscle changes in the elderly, according to the World Health Organization, and the most practical (and

low cost) measure for the evaluation of reserves of muscle tissue in the scenario and primary clinical care (Barbosa-Silva et al., 2016; Heymsfield et al., 2015; Kawakami et al., 2015; Landi et al., 2014; World Health Organization, 1995). The strengths of the study were the sample size and the fact that it was a pioneering study on the subject in the northern region of Brazil.

## 5. Conclusion

Sarcopenia was significantly associated with DM in the studied population, independent of other factors. This study helps to fill an important gap in the global vision of sarcopenia, mainly in reference to the Amazon region. However, prospective studies are necessary for better classification of the relationship between DM and sarcopenia, emphasizing the importance of adopting preventive measures against these pathologies and defining complications arising from this relationship.

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## Conflict of interest

None.

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