

ORIGINAL ARTICLE

doi.org/10.1590/S0004-2803.230402023-69

Diminished hand grip strength and cirrhosis: prevalence and associated factors

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HIGHLIGHTS

- This cross-sectional study seeks to evaluate the epidemiological distribution of diminished hand grip strength in cirrhotic patients at an outpatient clinic in Brazil, and its association with liver function and cirrhosis complications.
- A questionnaire was administered to patients and hand grip strength was measured using a dynamometer, with 3 interval measures taken for 3 seconds each.
- There was an association found between diminished hand grip strength and the female gender, and reduced hand grip strength and higher MELD scores.
- Therefore, the presence of reduced muscle strength in cirrhotic patients may be linked to prognostic factors and should be valued as clinical data in the management of these patients.

Received: 20 May 2023
Accepted: 1 August 2023

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
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ABSTRACT – Background – Sarcopenia is a syndrome characterized by progressive and generalized loss of muscle mass and strength, observed to varying degrees in patients with various chronic conditions. In cirrhotic patients, it reflects protein-energy malnutrition due to metabolic protein imbalance and is associated with worsened prognosis and reduced post-liver transplantation survival. **Objective** – To evaluate the epidemiological distribution of diminished hand grip (HG) strength in cirrhotic patients at an outpatient clinic of Santa Casa de Misericórdia in Vitória-ES, Brazil, seeking its association with liver function and cirrhosis complications. **Methods** – Cross-sectional, epidemiological, and single-center study. A questionnaire was administered to patients and HG strength was measured using a dynamometer, with three interval measures taken for 3 seconds each. **Results** – The study's total population was 64 cirrhotic patients, with a mean age of 58 years and alcohol as the most prevalent etiology. Reduced HG strength was defined based on two reference values: using cutoff point 1, reduced HG strength was identified in 33 patients (51.6%); according to cutoff point 2, 23 (35.9%) had reduced HG strength. The study showed that, among the parameters observed, there was an association between the female gender and diminished HG strength in both cutoff points. Additionally, it was noted that patients with a score of 15 or more on the Model for End-Stage Liver Disease (MELD) had decreased HG strength at cutoff point 2. The study showed no association between decreased HG strength and the occurrence of cirrhosis complications in the population studied. **Conclusion** – In our study, we obtained a diminished HG strength variation of 35–52%, which was related to higher MELD scores, suggesting an association with worse clinical outcomes. Therefore, the presence of reduced muscle strength in cirrhotic patients may be linked to prognostic factors and should be valued as clinical data in the management of these patients.

Keywords – Cirrhosis; sarcopenia; prognosis.

INTRODUCTION

In cirrhosis, as well as in most chronic diseases, a preferential loss of type II or fast fibers is expected. Although in vivo measurements of this type of fiber loss are still lacking in cirrhotic patients, there are signs of a sarcopenic process in many of these patients⁽¹⁾.

Cirrhosis is a significant cause of morbidity and mortality worldwide. It is worth noting that, since the disease affects people in their most productive years, there is a significant impact on the economy because of premature death, illness, and disability⁽²⁾.

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass, reduced muscle strength, and functional limitations⁽³⁾. It is a degenerative process common in the elderly and is associated with an increased occurrence of falls and fractures, as well as increased mortality⁽⁴⁾. It is prevalent in adults with neoplasms and patients with chronic diseases⁽³⁾.

In cirrhotic patients, sarcopenia reflects protein-energy malnutrition caused by an imbalance in protein metabolism⁽³⁾. This imbalance is multifactorial and includes increased fatty acid oxidation, decreased protein synthesis, increased amino acid consumption, increased gluconeogenesis, increased muscle proteolysis, and decreased caloric and protein intake^(1,5). This series of molecular changes causes protein catabolism to be much more significant than anabolism, resulting in muscle mass depletion. FIGURE 1, adapted from Ponziani⁽⁶⁾, exemplifies the

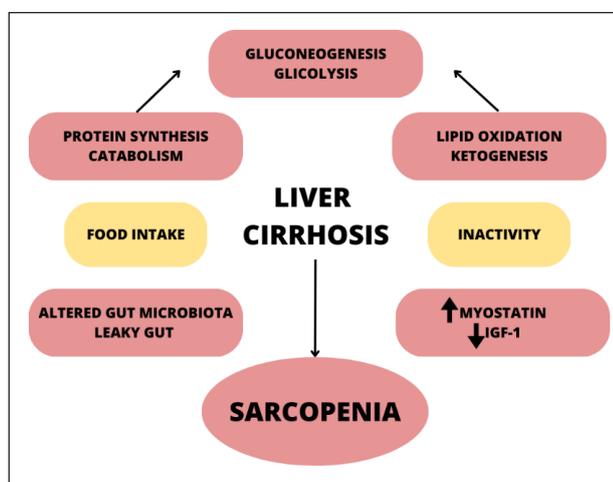


FIGURE 1. Factors responsible for sarcopenia in cirrhotic patients. Adapted from Sarcopenia in Patients with Advanced Liver Disease. Current Protein & Peptide Science 2018.

connections between the metabolic processes involved in sarcopenia development in cirrhotic patients.

One of the main limitations in understanding sarcopenia in cirrhotic patients is the difficulty in identifying a specific mediator of the interaction between the liver and muscle. Among potential mediators, hyperammonemia is significantly mentioned in studies since it signals impaired urea synthesis due to hepatic dysfunction and portosystemic circulation deficit. According to Dasarathy⁽¹⁾, ammonia accumulation in the muscle activates a series of molecular responses that are not fully understood, involving mitochondrial dysfunction and reduced adenosine triphosphate (ATP) production, leading to an adaptive response of autophagy of the muscle itself.

Malnutrition is a common condition in cirrhotic patients, affecting about 50% of decompensated patients and 20% of compensated patients⁽⁷⁾. Since malnutrition and sarcopenia are independent predictors of adverse clinical outcomes⁽⁸⁾, including survival, nutritional screening should be performed in all patients. FIGURE 2 presents a flowchart of screening of malnutrition in cirrhotic patients. Patients at risk of malnutrition should undergo a more detailed nutritional assessment to confirm the presence and degree of malnutrition, which is a potentially reversible condition⁽⁷⁾.

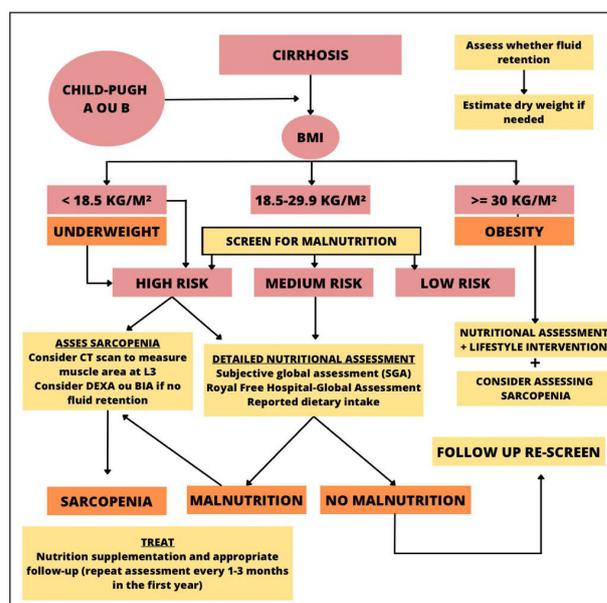


FIGURE 2. Flowchart of screening and management of malnutrition in cirrhotic patients.

Adapted from European Association for the Study of the Liver. EASL Clinical Practice Guidelines on nutrition in chronic liver disease.

Due to the lack of an effective method for measuring muscle functionality, the diagnosis of sarcopenia can be difficult in patients who present muscle loss but maintain little change in muscle strength. Currently, it is recommended to use at least two tests of muscle functionality for the diagnosis of skeletal muscle loss⁽⁵⁾.

Although few studies have directly compared different methods, the use of computed tomography of the psoas muscle is increasing, which allows visualization and quantification of skeletal muscle. Magnetic resonance imaging has also been proposed as a valuable method, although objective data on cirrhosis are scarce. In the Brazilian context, where a significant portion of services do not have imaging diagnostic machines, and prioritizing the rational use of resources is essential, another option for evaluating the presence of sarcopenia is the use of a dynamometer. A dynamometer is a tool that allows the evaluation of hand grip (HG) strength by measuring the maximum isometric force that can be exerted on the device, in a test called HG. This test functions as a general indicator of muscle strength and power and constitutes a low-cost and easily applicable tool.

The limited availability and high cost of certain diagnostic methods in Brazil limit investigative practice and complicate the diagnosis of sarcopenia. Therefore, our goal is to study diminished muscle strength and its relationship with epidemiological aspects of cirrhotic patients using simple yet effective tools, such as the HG strength test, seeking to deepen knowledge according to the Brazilian reality.

This study aims to analyze the prevalence of reduced HG strength in cirrhotic patients from an outpatient hospital service in Brazil. As secondary goals, we aim to investigate the association of diminished muscle strength in cirrhotic patients with hepatic function, as well as investigate the association of reduced HG strength with the occurrence of complications in these patients.

METHODS

This is a cross-sectional, epidemiological, and single-centered study. Data for analysis were collected between April 2021 and December 2021.

The population of interest consisted of patients of

both sexes, aged 18 years or older, diagnosed with cirrhosis, and who agreed to participate in the research by signing the Informed Consent Form (ICF). This study is in accordance with international ethical principles and was approved by the Brazilian Research Ethics Committee, with the title page number 44063520.0.0000.5065.

The study was conducted by approaching cirrhotic patients in the outpatient waiting room, applying a questionnaire with demographic data, and supplementing the information obtained about the patient with the records in their electronic medical records. After completing the questionnaire, the HG test was performed with a dynamometer, obtaining three measurements of the maximum force applied by the participant on the device for 3 seconds, using their dominant hand, separated by intervals of 30 to 60 seconds.

A qualitative and quantitative descriptive statistical analysis was applied to interpret the collected data. The data was organized in an EXCEL spreadsheet and later analyzed in the SPSS program version 27. Qualitative variables were analyzed using frequencies and percentages, while quantitative variables were analyzed using summary measures such as mean, median, and standard deviation.

Associations between variables were verified by the chi-square test or Fisher's exact test if expected values were less than 5. All inferential statistics were performed considering a significance level of 5%. All data was used exclusively for this study.

RESULTS

The main characteristics of the population studied are described in TABLE 1.

Two reference values were used to define the presence of diminished muscle strength based on the values obtained with the HG test. Initially, the reference value established by the updated European Working Group on Sarcopenia in Older People (EWGSOP II)⁽⁴⁾ was used, which defines cutoff values as a HG test of less than 27 kg for men and less than 16 kg for women. Based on this cutoff point (cutoff point 1), diminished muscle strength was identified in 33 patients (51.6%).

At another moment, the reference values esta-

TABLE 1. Demographic characteristics of the studied population.

		Frequency (n)	Percentage
Sex	Feminine	21	32.8%
	Masculine	43	67.2%
Etiology*	Alcohol	32	50%
	Hepatitis C	13	20.4%
	Hepatitis B	12	18.8%
	Others	11	17.3%
Ascites	No	47	73.4%
	Yes	17	26.6%
Encephalopathy	No	58	90.6%
	Yes	6	9.4%
Ascites and encephalopathy	No	56	87.5%
	Yes	8	12.5%
Smoking	No	52	81.3%
	Yes	12	18.8%
Comorbidities	No	16	25.0%
	Yes	48	75.0%
Child-Pugh	A	43	67.2%
	B	16	25.0%
	C	5	7.8%
MELD 1**	<15	53	82.8%
	>=15	9	14.1%
MELD 2**	<20	59	92.2%
	>=20	3	4.7%
Population	Total	64	100%

*Most patients had a record of a sum of etiologies, all of which were accounted for in the study, therefore there was the possibility of more than one etiology for the same cirrhotic patient; **It is clear that MELD 1 is considering the cutoff point at 15 and MELD 2, in turn, at 20.

blished by the Budziareck study⁽⁹⁾, conducted in a Brazilian population, were applied. Budziareck defines the cut-off line for reduced muscle strength as the 5th percentile value in each group, presented in TABLE 2.

TABLE 2. 5th percentile value of handgrip strength with the dominant hand according to sex and age, adapted from Budziareck⁽¹⁶⁾.

Age	5th percentile value (Kg)	
	Man	Woman
18–30 years	30	16
31–59 years	27	16
60 years or older	18	11

The population of this study was organized by age group according to the values cited by Budziareck⁽⁹⁾, resulting in 1 (1.6%) participant aged 18 to 30 years, 32 (50%) participants aged 31 to 59 years, and 31 (48.4%) aged 60 years or older. Using Budziareck⁽⁹⁾ as a reference, cut-off point 2 was created to identify the presence of reduced muscle strength. A total of 23 (35.9%) participants had diminished muscle strength. TABLE 3 compares diminished muscle strength distribution according to both cutoff points used in this study.

TABLE 3. Comparing diminished muscle strength in the population studied according to both cutoff points.

Diminished muscle strength	Cutoff point 1*	Cutoff point 2**
Absent	31 (48.4%)	41 (64.1%)
Present	33 (51.6%)	23 (35.6%)
Total	64 (100%)	64 (100%)

*EWGSOP II: hand grip values <27 kg in men and <16 kg in women; **Budziareck: hand grip values <5th percentile of each group.

DISCUSSION

Even though large projects investigate the association of sarcopenia with chronic liver disease, there is still no clear consensus regarding its true prognostic value in cirrhotic patients. The existence of a series of unanswered questions regarding sarcopenia in cirrhotic patients arouses curiosity and emphasizes the importance of scientific work carried out on the subject.

Our study showed that among the parameters observed (gender, etiology of cirrhosis, cirrhosis complications, comorbidities, smoking, Child-Pugh classification, and MELD score), only gender and MELD indicators were relevant. TABLE 4 compares the proportion of reduced muscle strength according to the two cutoff points used in the study, and its relationship with the different aspects observed.

After analyzing the results obtained from comparing individuals with reduced muscle strength and their gender, it was observed that there was significance ($P=0.006$) between the above-mentioned association, with a predominance of females in patients with diminished HG strength in both cutoffs 1 and 2. According to the meta-analysis performed by Lowe⁽¹⁰⁾, literature in general shows that male

TABLE 4. Diminished muscle strength according to the two cutoff points used in the study, and its relationship with the different aspects described below.

		Diminished muscle strength by cutoff 1	Diminished muscle strength by cutoff 2
Gender	Male	17 (26.5%)	10 (15.6%)
	Female	16 (25%)	13 (20.3%)
Etiology	Alcohol	13 (20.3%)	9 (14%)
	Viral hepatitis (B and C)	13 (20.3%)	9 (14%)
Complication	Ascites	8 (12.5%)	6 (9.3%)
	Encephalopathy	4 (6.2%)	2 (3.1%)
	Both	5 (7.8%)	3 (4.6%)
Comorbidities	Yes	24 (37.5%)	15 (23.5%)
	No	9 (14%)	8 (12.5%)
Smoking	Yes	6 (9.3%)	5 (7.8%)
	No	27 (42.1%)	18 (28.1%)
Child-Pugh	A	20 (31.2%)	13 (20.3%)
	B or C	13 (20.3%)	10 (15.6%)
MELD	> or = 15	6 (9.3%)	17 (26.6%)
	> or = 20	1 (1.6%)	1 (1.6%)

patients have higher mortality when sarcopenia and gender are associated, however, a study showed that the performance of female patients in muscle functionality tests (grip strength) is lower than that of male patients, and gender is an efficient marker for sarcopenia.

As a matter of fact, few studies relate gender to sarcopenia, requiring further research on the association. Furthermore, a possible explanation for this phenomenon lies in the existence of specific estrogen hormone-responsive receptors in skeletal muscle, which stimulate the proliferative activity of muscle satellite cells and regenerate muscle tissue⁽¹¹⁾. Thus, during the perimenopause and menopause period, the decline in estradiol levels would lead to a decrease in this regenerative capacity of muscle fibers, resulting in long-term loss of muscle mass and strength⁽¹²⁾, as well as an increase in visceral adiposity and a decrease in bone density⁽¹¹⁾. These factors significantly contribute to the development of the condition called “sarcopenic obesity,” characterized by a sarcopenic clinical picture and excess body weight.

In addition, estradiol is involved in modulating local and systemic inflammatory responses, favoring catabolic processes, and contributing to the establishment of sarcopenia^(11,12). Considering that 48.4% of the study participants were over 60 years of age, the predominance of women in the perimenopausal or postmenopausal age range in this study is noteworthy,

and therefore, the possibility of sarcopenia also being associated with characteristic hormonal changes of this period cannot be ruled out. On the other hand, a meta-analysis performed by Lowe demonstrates that estrogen levels are elevated in women with cirrhosis compared to healthy controls, however, their overall significance and potential impact on muscle homeostasis require further investigation⁽¹⁰⁾.

In this study, the presence of a MELD score greater than or equal to 15 had a significant association ($P=0.047$) with reduced muscle strength, as cirrhosis is the characterization of the advanced stage of chronic liver disease and this group of patients often develops protein-energy malnutrition. These changes involve modifications in cellular physiology and immunity, leading to clinical repercussions such as decreased survival and increased morbidity.

Another liver disease assessment scale that was investigated for its relationship with reduced HG strength was the Child-Pugh (CP) classification, which is used to predict mortality in cirrhotic patients. However, this association was found to be non-significant. Therefore, it can be inferred that diminished muscle strength can occur in patients with good liver function, such as those classified as CP A, as well as in patients with more severe liver dysfunction, such as those classified as CP B and C. This finding does not contradict the association between the presence of sarcopenia and liver dysfunction re-

sulting from cirrhosis but rather demonstrates that this relationship is not proportional to the degree of liver impairment, highlighting the need for attention to metabolic dysfunctions in all cirrhotic patients, not just those with worse liver function.

The relationship between diminished HG strength and the most common etiologies of cirrhosis in the studied population (alcohol and viral hepatitis) was shown to be not significant, as the *P*-value was 0.473 for cutoff point 1 and 0.245 for cutoff point 2. This finding is supported by a meta-analysis conducted by Gao⁽¹³⁾. However, it is interesting to note that, as mentioned by Saeki⁽¹⁴⁾, ethanol inhibits protein synthesis in muscle fibers, which can result in skeletal muscle autophagy and consequent loss of muscle mass. In addition, excessive alcohol consumption leads to accelerated proteolysis, which should contribute even more to the development of sarcopenia⁽¹⁵⁾. Therefore, further studies are needed to determine the true role of alcoholism in the development of sarcopenia.

Regarding the complications of cirrhosis studied (ascites and hepatic encephalopathy), no significant associations were found with the presence of reduced muscle strength in any of the groups in this study: patients with ascites, patients with encephalopathy, and patients with ascites and encephalopathy. However, according to Tantai's study⁽¹⁶⁾, complications associated with cirrhosis, such as the presence of ascites, hepatic encephalopathy, and hepatorenal syndrome, were observed and strongly correlated with the presence of sarcopenia. Among the results obtained by Tantai⁽¹⁶⁾, sarcopenia was found to increase the risk of ascites by 3.78 times.

Finally, the last factor studied that was not found to have a relevant relationship with diminished HG strength was smoking. However, Gao⁽¹³⁾ contrasts with this data by including smoking among the factors associated with sarcopenia, which can be explained by the fact that smoking induces catabolism and therefore contributes to the loss of muscle mass. Therefore, it is still unclear whether smoking is relevant regarding the presence of reduced muscle strength in cirrhotic patients, which is a question that can be clarified by future studies in the field.

It is important to highlight that, due to limitations of the research method used in this study, such as the limited number of patients from the service, the identification of a significant association of sarcopenia in cirrhotic patients with the studied variables may have been lower than the real association, as the population involved in this study was small. The need for more projects focused on understanding the factors involved in the development of sarcopenia in patients with chronic liver diseases is emphasized.

CONCLUSION

In our study, a variation between 35–52% of diminished muscle strength was obtained using the HG test in the cirrhotic population studied. There was an association between the prevalence of reduced muscle strength and female gender (51.5% according to cutoff 1; and 43.5% according to cutoff 2), as well as an association between diminished HG strength and MELD score greater than or equal to 15 (18.8% based on cutoff 1 parameters; and 73.9% when considering cutoff 2).

Therefore, the presence of reduced muscle strength in cirrhotic patients may be linked to important prognostic factors that should be valued in the management of these patients.

Additionally, no significant associations were found between diminished HG strength and cirrhosis complications in our study.

Authors' contribution

Andrade CPT, Dalcumune LF, Fiorese NM: data collection, search execution, and writing of the project. Trindade LZ, Ferreira FB, Pacheco MP: mentoring, and final review of the project.

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Andrade CPT, Dalcumune LF, Fiorese NM, Trindade LZ, Ferreira FB, Pacheco MP. Diminuição da força no teste de Hand Grip e cirrose hepática: prevalência e fatores associados. *Arq gastroenterol.* 2023;60(4):431-7.

RESUMO – Contexto – Sarcopenia é uma síndrome caracterizada por perda progressiva e generalizada de massa e força muscular, observada em diferentes graus em pacientes com afecções crônicas diversas. Nos cirróticos, reflete uma desnutrição proteico-energética por desequilíbrio metabólico de proteínas, e associa-se ao pior prognóstico e redução da sobrevida pós transplante hepático. **Objetivo** – Avaliar a distribuição epidemiológica da diminuição da força no teste de Hand Grip (HG) nos pacientes cirróticos do ambulatório da Santa Casa de Misericórdia de Vitória-ES, buscando sua associação com a função hepática e complicações. **Métodos** – Estudo transversal, epidemiológico e unicêntrico. Aplicou-se um questionário aos pacientes e mediu-se a força de preensão manual HG com o auxílio de um dinamômetro, sendo realizadas 3 medidas intervaladas durante 3 segundos cada. **Resultados** – A população total foi de 64 pacientes cirróticos, sendo a média de idade 58 anos e a etiologia mais prevalente o álcool. Definiu-se a presença de redução da força do HG a partir de dois valores de referência: com base no ponto de corte 1, a redução da força do HG foi identificada em 33 pacientes (51,6%); pelo ponto de corte 2, 23 (35,9%) tinham diminuição da força do HG. O estudo evidenciou que, dentre os parâmetros observados, houve associação entre o sexo feminino e a diminuição da força no teste de HG nos dois pontos de corte. Além disso, notou-se que pacientes com pontuação de 15 ou mais no Modelo para Doença Hepática Terminal (MELD) tiveram mais redução da força do HG de acordo com o ponto de corte 2. O estudo evidenciou que não houve associação entre a diminuição da força no teste de HG e o evento de complicações da cirrose na população estudada. **Conclusão** – Em nossa casuística, obtivemos uma variação da diminuição da força muscular entre 35-52% pelo teste de HG, o que teve relação com o MELD mais elevado, podendo demonstrar associação com piores desfechos clínicos. Dessa forma, concluiu-se que a presença de diminuição da força muscular no teste de HG nos cirróticos pode estar ligada a fatores prognósticos, e deve ser valorizada como dado clínico no manejo destes pacientes.

Palavras-chave – Cirrose; sarcopenia; prognóstico.

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