Usefulness of Gait Speed as a Screening Parameter for Sarcopenia in Cirrhotic Patients Marwa Abdel Razek Salama^{*1}, Elham Ahmed Hassan¹, Nahed A Makhlouf¹, Mohamed Eltaher Ibrahim¹, Hany M Dabbous², Medhat A Salah³, Hani Sayed Aboalam⁴, Mohamed Zidan Mohamed⁵

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ABSTRACT

Background: Sarcopenia in cirrhotic patients has a serious effect on their outcome. Although several modalities are used for diagnosing sarcopenia by measuring skeletal muscle mass, they are expensive and may not be available. The objective of the present study is to assess the utility of gait speed for diagnosing sarcopenia in cirrhosis as compared with computed tomography skeletal muscle index (CT-SMI). **Patients and methods:** A cross-sectional study recruited 331 adult patients with hepatitis C-related cirrhosis. Clinical assessment, gait speed, and CT-SMI in the third lumbar vertebra were determined. Sarcopenia was defined when CT-SMI < 52.4 cm2/m2 in men and when < $38.5 \text{ cm}^2/\text{m}^2$ in women. Diagnostic performance of gait speed at a cut-off value <0.8 m/s for diagnosing sarcopenia in cirrhosis was assessed. **Results:** Sarcopenia by CT-SMI was detected in 52.6% of patients. A significant correlation was found between CT-SMI and gait speed with slightly higher in women. Using the existing cut-off value of gait speed lower than 0.8 m/s, we detected sarcopenia in 146 (44.1%) patients, and when compared with CT-SMI for diagnosing sarcopenia, the specificity, sensitivity and overall accuracy were 91.7%, 84.5%, and 87.9%, respectively. Better performance was observed in women; 82.5% sensitivity, 96.1% specificity and 91.4% accuracy. **Conclusion:** Gait speed could be used as a marker of sarcopenia for cirrhotic patients in areas where modalities of diagnosing skeletal muscle index are deficient. Although gait speed is not the only method for diagnosing sarcopenia, it has the potential to be a helpful clinical tool for identifying sarcopenic patients.

Keywords: Gait speed, Liver cirrhosis, Sarcopenia, Skeletal muscle index.

INTRODUCTION

Sarcopenia is the progressive wasting away of muscular mass and function, manifesting itself in diminished performance or strength ⁽¹⁾. The incidence among cirrhotic individuals ranges from 40-70%, depending on the severity of the underlying liver disease and the diagnostic methods and criteria employed ^(2,3). Loss of muscle mass and strength is also linked to physical frailty, which can render patients immobile and restrict their outdoor activity ⁽⁴⁾.

Sarcopenia is implicated in the pathogenesis of decompensation in liver cirrhosis and is linked to worse outcomes like decreased quality of life, increased risk of cirrhosis complications, infections, hospitalizations, and mortality⁽⁵⁾. For this reason, the early detection and proper management of sarcopenia in cirrhotic patients are crucial for the potential improvement of survival⁽⁶⁾.

Several works evaluated sarcopenia in cirrhosis with different modalities including bioelectrical impedance analysis (BIA), Dual Energy X-ray Absorptiometry (DXA), magnetic Resonance Imaging (MRI), ultrasonography, and computerized tomography (CT) scan which may not available in clinical locations besides anthropometric parameters ^(2,6,7). Furthermore, these modalities cannot be used routinely for the clinical diagnosis of sarcopenia due to both cost and access difficulties ⁽⁸⁾. On the other hand, anthropometric parameters are less expensive but more prone to error ⁽⁹⁾. The most commonly used and thoroughly studied measure of sarcopenia in people with cirrhosis is computed tomography (CT), which is also the most expensive tool for detecting sarcopenia ^(2,5). There is some radiation exposure involved, and special software

is needed to determine how much of a CT scan is devoted to muscle before making any adjustments ⁽¹⁰⁾.

On the other hand, gait speed has been considered a simple, objective, and disease-specific measuring parameter of physical performance in several diseases e.g., chronic obstructive pulmonary disease, as well as chronic kidney disease ^(11,12). Hospitalization for these disorders' consequences is also linked to this ⁽¹³⁾.

Several studies revealed a link between muscle performance or motor function and liver diseases (14,15) particularly non-alcoholic steatohepatitis Moreover, the cut-off values used to define sarcopenia and reduced muscle function by gait speed were validated in several conditions e.g., patients with tumors and obesity ^(16,17), but their utility in cirrhotic patients particularly those with hepatitis C virus (HCV)-related cirrhosis that is more prevalent in our locality is lacking. Therefore, the purpose of this study was to investigate the validity of using speed gait as a screening tool for sarcopenia in cirrhotic patients by examining the association between muscular function as determined by gait speed and skeletal mass index (SMI) as assessed by CT scan.

PATIENTS AND METHODS

This cross-sectional study was conducted at Assiut University Hospital, Assiut, Egypt, from August 2018 to December 2021.

Study population

The study population included 331 adult patients, diagnosed with cirrhosis due to hepatitis C who were hospitalised at the AL-Rajhi Liver Center at Assiut University Hospital in Assiut, Egypt. The diagnostic criteria for cirrhosis were met in all patients based on clinical, biochemical, and imaging results. Child-Pugh and Model for End-Stage Liver Disease - sodium (MELD Na) scores were used to determine the level of cirrhosis ^(18,19). Patients with non-HCV-related cirrhosis, human immunodeficiency virus, tuberculosis malignancies, chronic debilitating diseases such as, chronic obstructive pulmonary disease, chronic renal failure, neuromuscular disorders, inflammatory bowel disease, congestive heart failure and those receiving anabolic steroids were excluded.

Methods

A complete medical history and physical was conducted for all participants before including in the study. Laboratory investigations included liver function tests, international randomized ratio (INR), serum creatinine, and sodium. Thereafter, anthropometric measurements including body mass index (BMI), and CT scan were done. Finally, the four-meter gait speed test was performed.

Body mass index (BMI)

The body mass index was determined by dividing the subject's weight in kilos by the square of their height (meters) in kg/m^2 with the normal range in adults between 18.5 - 24.9 kg/m² (²⁰⁾.

Four-meter gait speed (4-m gait speed)

The National Institutes of Health used a 4-meter gait speed test to determine gait velocity ⁽²¹⁾. Each participant was given a standing start and then asked to walk four meters at their normal pace while identifying landmarks; their speed was recorded in meters per second (m/s). For patients who are unable to walk at all (i.e., non-ambulatory), the gait speed is set to zero ⁽²²⁾. According to **Cruz-Jentoft** *et al.* ⁽¹⁾, sarcopenia was defined at a cut-off value of Gait speed < 0.8 m/s.

Computer Tomography- skeletal muscle index (CT-SMI)

Skeletal muscle index (SMI) (cm² /m²) was calculated by dividing the patient's height squared by their cross-sectional muscle area (cm2) from a CT scan taken at the level of the third lumbar vertebra (L3). This was done using the National Institutes of Health ImageJ software. According to **Prado** *et al.* ⁽²³⁾, sarcopenia was assessed when CT-SMI a < 52.4 cm²/m² in men and when <38.5 cm²/m² in women.

Ethical considerations

Assiut University Hospital's Local Ethics Committee gave its seal of approval to the study (IRB No: 17200236). All participants were given a thorough description of the study's goals, procedures, potential associated risks, and side effects, and asked to sign an informed consent form before being enrolled. The work has been conducted in accordance with the principles of the World Medical Association's code of ethics (Human subjects research must adhere to the Declaration of Helsinki. The study was registered on clinical trials.gov with NCT03629444.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 18 for Windows® (IBM SPSS Inc, Chicago, IL, USA). To ensure that the data were normally distributed, we employed the Shapiro-walk test. Student's t-test was used to compare quantitative variables expressed as means and SD or medians and ranges. The chi-squared (χ^2) or Fisher's exact probability test was used to make comparisons between qualitative data expressed as a percentage. Pearson's correlation coefficient was used to ascertain how strongly the variables were linked to one another. The degree of correlation between the variables was calculated using Pearson's correlation coefficient. Prediction of sarcopenia in cirrhosis was performed using multiple regression analysis. The sensitivity, specificity, positive (PPV), and negative (NPV) predictive values, positive (+) likelihood ratios (LR), and overall accuracy of gait speed in diagnosing sarcopenia were determined by plotting receiver operating characteristic (ROC) curves. Because we maintained a 95% confidence interval around our results, we regarded a P-value of 0.05 to indicate statistical significance.

RESULTS

A total of 331 patients who have HCV-related cirrhosis (116 women and 215 men and with a mean age of 56.2 (SD 13.5) years were assessed. Their characteristics were shown in Tables (1 and 2) where sarcopenia recognized by CT-SMI was detected in 174 (52.6%) patients (40 women and 134 men). Results showed that both women and men with cirrhosis in Child-Pugh class C had slower gait speeds and poorer CT-SMI values compared to those in Child-Pugh classes A and B as shown in Figure 1 (a and b).

Table (1):	Characteristics	of	the	study	cirrhotic
patients					

Variable	Patients (n= 331)	Women (n= 116)	Men (n= 215)	P-value
BMI (kg/m ²)	24.3 ± 6.2	26.3 ± 5.5	23.2 ± 6.3	< 0.001
Gait speed (m/s)	$\begin{array}{c} 0.82 \pm \\ 0.37 \end{array}$	0.92 ± 0.32	0.76 ± 0.37	< 0.001
Sarcopenia by gait speed (%)	146 (44.1)	33 (28.4%)	113 (52.6)	<0.001
CT-SMI (cm ² /m ²)	43.7 ± 6.8	39 ± 3.9	46.2 ± 6.7	< 0.001
Sarcopenia by CT-SMI (%)	174 (52.6)	40 (34.5)	134 (62.3)	<0.001

Data were expressed in form of mean \pm SD and frequency (percentage) in the case of nominal data. P-value <0.05 was significant. BMI: body mass index; CT: computed tomography; SMI: skeletal muscle index. Sarcopenia was defined by CT-SMI < 38.5 cm²/m² in women and < 52.4 cm²/m² in men and gait speed < 0.8 m/s.

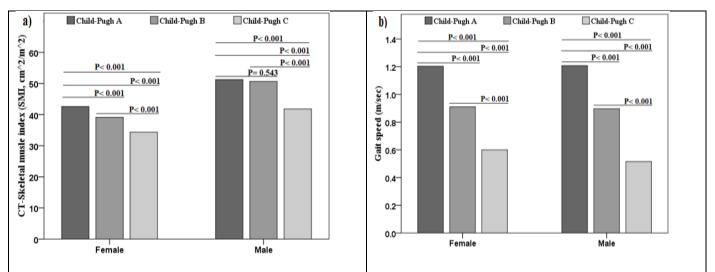


Figure (1): Distribution of a) CT-SMI and b) gait speed in female and male patients according to Child-Pugh classification

Table (2): Comparison of demographics and clinical characteristics between cirrhotic patients with and without
sarcopenia identified by CT-SMI

Variable	Total cirrhotic patients (n= 331)	Patients without sarcopenia (n= 157)	Patients with sarcopenia (n= 174)	P-value
Age (years, range)	56.2 ± 13.5 (18-81)	$54.9 \pm 12.1 \\ (18 - 80)$	57.4 ± 14.6 (20 - 81)	0.096
Sex female /male (%)	116/215 (35/65)	76/81 (48.4/51.6)	40/134 (23/77)	< 0.001
Duration of diagnosis (years)	4 (1 - 21)	3 (1 - 21)	5 (2 -15)	< 0.001
Co-morbid diseases (%)	121 (36.6)	59 (37.6)	62 (35.6)	0.713
BMI (kg/m ²)	24.3 ± 6.2	27.7 ± 6.4	21.2 ± 4	< 0.001
Ascites (%)	174 (52.6)	14 (8)	160 (92)	< 0.001
Serum albumin (g/dl)	2.8 ± 0.8	3.3 ± 0.6	2.3 ± 0.7	< 0.001
Serum bilirubin (mmol/l)	18.7 ± 4.1	15 ± 3.51	22.5 ± 4.7	0.002
ALT (U/L)	40 ± 8.7	30 ± 7.6	50 ± 12.5	< 0.001
INR	1.4 ± 0.4	1.2 ± 0.2	1.5 ± 0.4	< 0.001
Serum creatinine (µmol/L)	102.2 ± 40	87.2 ± 27.5	115.8 ± 44.5	< 0.001
Child-Pugh score	8.7 ± 2.5	7 ± 2	10 ± 2	< 0.001
Child-Pugh class (A/B/C) (%)	81/34/146 (24.5/10.3/44.1)	67/79/11 (42.7/50.3/7)	14/25/135 (8/14.4/77.6)	< 0.001
MELD Na score	25.2 ± 6.3	22.76 ± 5.28	27.45 ± 6.27	< 0.001
Gait speed (m/s)	0.81 ± 0.36	1.05 ± 0.23	0.6 ± 0.33	< 0.001

Both women (Figure 2a) and men (Figure 2b) showed a direct positive association between CT-SMI and gait speed. The correlation was slightly stronger in women. The association between women's gait speed and standard movement index (SMI) was 0.729 according to Pearson correlation coefficient (r) (P<0.001). The male version of the Pearson correlation coefficient (r) was 0.648 (P<0.0001).

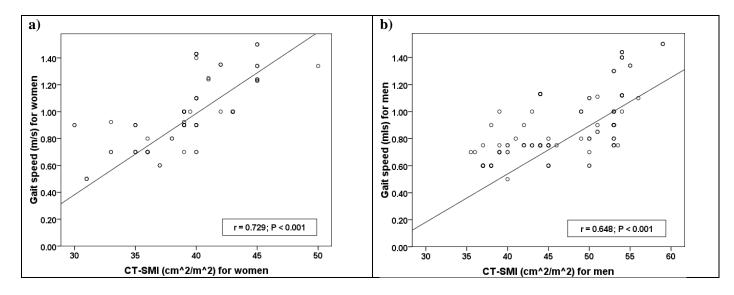


Figure (2): Correlation between gait speed and CT-SMI in a) female and b) male patients. CT- SMI: Computed tomography-skeletal muscle index.

We discovered that sarcopenia was more common in male patients than female patients using univariate analysis (P<0.001). In addition, sarcopenia was associated with prolonged disease duration, ascites, and severity of liver disease by Child-Pugh, and MELD-Na scores (P<0.001). Serum bilirubin, ALT, INR, and creatinine were all significantly greater in patients with sarcopenia, but serum albumin and body mass index were significantly lower (P<0.001).

Multiple regression analysis was performed with the variables from the univariate analysis that required to be significantly correlated with sarcopenia in order to determine which factors might independently predict the presence of sarcopenia. (P<0.05), If the Child-Pugh score indicates a higher degree of liver cirrhosis (P<0.001), elevated ALT, and decreased gait speed were independent predictors for sarcopenia in patients with cirrhosis.

By means of the existing cut-off value of gait speed <0.8 m/s⁽¹⁾, sarcopenia was detected in 146 (44.1%) cirrhotic patients, and when compared with CT-SMI results for diagnosing sarcopenia, the sensitivity, specificity, PPV, NPV, +LR, -LR and overall accuracy were 84.5%, 91.7%, 91.9%, 84.2%, 10.2, 0.17 and 87.9% respectively with AUC of 0.902 (0.864-0.932). For women, gait speed had AUC of 0.959 (95%CI: 0.905-0.987), sensitivity of 82.5%, specificity of 96.1%, PPV of 91.8%, NPV of 91.2%, +LR of 20.9, +LR of 0.18 and overall accuracy of 91.4% at the cut-off < 0.8 m/s (Figure 3a). For men, gait speed had an AUC of 0.877 (95%CI: 0.826-0.918), a sensitivity of 83.6%, specificity of 87.7%, PPV of 91.8, NPV of 76.4%, +LR of 6.8, -LR of 0.19 and the overall accuracy of 85.1% at the same cut-off (Figure 3b).

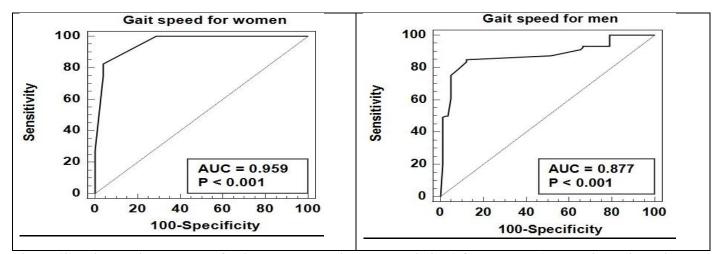


Figure (3): Diagnostic accuracy of gait speed to predict sarcopenia in a) female and b) male cirrhotic patients.

DISCUSSION

Patients with cancer and chronic conditions like cirrhosis are at increased risk for developing sarcopenia, a clinical condition defined by a gradual loss of skeletal muscle mass and strength. Sarcopenia is a reflection of protein-energy deficiency and is used as a quantitative, objective, and straightforward indicator of a patient's nutritional condition. Even after liver transplantation (LT), sarcopenia in cirrhosis has emerged as an independent indicator of poor outcome ^(6,10).

Although several modalities are used for diagnosing sarcopenia by measuring skeletal muscle mass, they are expensive and may not be available ^(2,6,7). Therefore, this study aimed to assess the utility of gait speed per se as a unique simple tool for screening of sarcopenia in cirrhotics to reduce the number of patients requiring expensive muscle mass measurements.

Our analysis identified sarcopenia based on CT-SMI in 52.6% of 331 patients with HCV-related cirrhosis where the majority of cases were men (77%) that were compatible with the results of an Egyptian study of **Khattab** *et al.* (52.5%) ⁽²⁵⁾. Moreover, our result was within the range reported in a systematic review where it was $(24.8 - 70\%)^{(4)}$. It was higher than that reported by **Erkan** *et al.* (39.7%) ⁽²⁶⁾, and lower than that reported by **Hanai** *et al.* (68%) ⁽²⁷⁾. Additionally, these studies revealed that sarcopenia appeared more among men ^(4,27). This discrepancy in the frequency of sarcopenia may be multifactorial including variable definitions of sarcopenia, study design, and sample size.

In the current study, muscle function estimated by gait speed correlated with muscle mass quantified by CT-SMI, both in males and females. Moreover, gait speed, as well as CT- SMI, decreased with increased severity of cirrhosis. These findings were consistent with previous studies exploring that muscle function and muscle mass may play roles in the development of sarcopenia ^(15,28).

Similar to previous studies $^{(27,29)}$, Gait speed was lower (0.6 m/s) in the sarcopenia group than in the nonsarcopenia group (1.05 m/s). Patients with cirrhosis were more likely to experience sarcopenia if they had an elevated ALT, a higher Child-Pugh score, and impaired muscle function (low gait speed). Muscle weakness, especially in the lower extremities, may be caused by the progression of liver fibrosis and contribute to slow walking speed ⁽³⁰⁾. Gait speed is an important means of assessing motor function and has been used as a diagnostic criterion for sarcopenia by different groups ^(1,31).

We assessed the diagnostic yield of gait speed to predict sarcopenia in cirrhotic patients at the usual cutoff value (<0.8 m/s) that was used to identify sarcopenia in geriatrics ⁽¹⁾. It had a good diagnostic yield with higher performance in women where AUC was 0.959 (95%CI: 0.905-0.987), sensitivity and specificity were 82.5% and 96.1% respectively. Poor muscle function has been reported by many authors to be a reliable test to indicate sarcopenia ^(32,33). At the mentioned cut-off value, 44.1% of cirrhotic patients had sarcopenia and the majority was men (52.6%). Loss of muscle strength or performance in cirrhotic patients may be attributable to intramuscular fat buildup and other biological abnormalities in muscle structure, but these changes cannot be determined by measuring muscle mass (e.g., SMI using cross-sectional imaging), a static measure ⁽³⁴⁾. Muscle atrophy and weakness in the elderly were shown to be more strongly linked to physical impairments and limitations in daily functioning than to overall body mass ⁽³⁵⁾. Thus, muscle strength or function is increasingly being recognized as more important than skeletal muscle mass alone ⁽¹⁴⁾.

The study's limitations stem from its crosssectional, single-center design, which restricted the researchers' ability to show a connection between muscles mass as measured by CT-SMI and muscle function as measured by gait speed. Therefore, extensive multicenter studies are needed to confirm these results and validate gait speed's use in sarcopenia diagnosis, as well as to identify cut-off points for this parameter that are representative of the cirrhotic community.

In conclusion, gait speed could be used as a marker of sarcopenia for cirrhotic patients in areas where modalities of quantifying skeletal muscle mass are deficient. At the existing cut-off value (<0.8m/s), gait speed had a good diagnostic yield in predicting sarcopenia in cirrhosis with higher performance in women. Although gait speed is not the only method for diagnosing sarcopenia, having a strong association with CT-skeletal muscle index, it may be a helpful clinical tool for identifying patients at risk of sarcopenia.

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Author contribution: Authors contributed equally in the study.

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