Abbasy *et al. Egyptian Liver Journal* (2023) 13:31
https://doi.org/10.1186/s43066-023-00265-9

Egyptian Liver Journal

ORIGINAL RESEARCH ARTICLE

Open Access

Prognostic and diagnostic anthropometric biomarkers of sarcopenia in a cohort of Egyptian patients with hepatitis C-induced liver cirrhosis

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Abstract

Background Chronic hepatitis C (HCV) infection is a leading cause of liver cirrhosis (LC) worldwide with decompensation-related clinical sequelae. Sarcopenia is currently recognized as a fundamental complication of LC owing to various mechanisms. This study aimed to assess the role of anthropometric measures of sarcopenia in predicting the outcome of LC as assessed by the Child-Turcotte-Pugh (CTP) grade.

Results A cross-sectional study was carried out on 80 patients with HCV-related LC with different CTP grades. The diagnosis of sarcopenia was based on the 2018 definition of sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP). Muscle strength was assessed by hand grip strength (HGS) and lower leg extension strength (LES). Assessment of muscle mass was performed by measuring mid-calf circumference (MCC) and mid-arm muscle circumference (MAMC). HGS varied significantly between the different CTP grades, being highest in CTP grade C. Additionally, the number of patients diagnosed with "definitive sarcopenia" using either HGS/MCC or LES/MCC varied significantly between CTP grades, being highest in CTP grade C.

Conclusions HGS is a better predictor of worse outcomes of liver cirrhosis than LES. The combination of MCC and HGS or LES is a potentially promising noninvasive prognostic biomarker of liver disease.

Keywords Sarcopenia, Anthropometry, HCV, Liver cirrhosis, Prognosis, Outcome, Morbidity, Child–Pugh score

Background

Chronic hepatitis C (HCV) infection is an important cause of liver-related morbidity and mortality owing to liver cirrhosis (LC), parenchymal and mesenchymal dysfunction with hepatic encephalopathy (HE), and hepatocellular carcinoma (HCC) as the major clinical sequelae [1].

Diverse methods have been checked, considered, and proposed for assessing the outcome and prognosis of cirrhosis, the most conventional scoring system is the CTP scoring system. It relies on five parameters, namely, HE, ascites, serum bilirubin, serum albumin, and international normalized ratio (INR), and classifies LC accordingly into three grades A, B, and C [2]. Shortcomings for the CTP scoring system, such as subjective assessment of ascites as well as intellectual impairment, rendered the score erroneous and mandated validation of novel scores [3].

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Sarcopenia, characterized by a decline in muscle mass, strength, and/or physical performance, is prevalent not only in the elderly population but also as a complication in patients with LC. Inadequate nutrient absorption, impaired synthetic capacity of hepatic cells and increased protein catabolism are the proposed culprits in the loss of muscle volume in advanced liver disease. In the cirrhotic population, sarcopenia was found to correlate positively with altered ammonia detoxification, hyperammonemia and HE without subjective bias [4].

To date, no universal definition for sarcopenia in patients with liver cirrhosis is standardized. Nonetheless, the European Working Group on Sarcopenia in Older People (EWGSOP), which incorporates muscle strength and mass in addition to performance assessment, provides an auspicious clinical definition [5].

Computed tomography (CT) and dual energy X ray absorptiometry (DXA) are the gold-standard methods to diagnose sarcopenia [6, 7]. Anthropometry, however, is an accurate, yet inexpensive, noninvasive method for muscle mass and nutritional status evaluation that was found to correlate to CT and DXA findings and hence can by be utilized as surrogate biomarkers for sarcopenia diagnosis [8].

The current work was performed to assess the role of anthropometric measures of sarcopenia in the diagnosis and prediction of the outcome of liver cirrhosis as assessed by CTP grade among a cohort of Egyptian patients with HCV-induced LC.

Patients and methods

This cross-sectional observational study included all consecutive patients with HCV-related LC who met the inclusion criteria and were admitted to the Tropical Medicine Department, at the Alexandria Main University Hospital, during the period from June to December 2020. Patients were recruited after approval of the local Ethical Review Committee. All patients signed an informed consent regarding the nature and aim of the study. Also, written informed consent for publication was obtained.

The inclusion criteria were patients with HCV-related decompensated (LC) aged between 18 and 60 years old. Patients with chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), hepatocellular carcinoma (HCC) and individuals > 60 years old were excluded from the study.

All study participants were subjected to detailed history taking, thorough clinical examination and laboratory investigations, including complete blood picture (CBC), fasting blood glucose (FBG), serum levels of alanine transaminase (ALT), aspartate transaminase (AST), prothrombin time, INR, total and direct bilirubin, albumin, urea, and creatinine. Moreover, HCV infection was diagnosed by the presence of serum anti-HCV antibody (HCV Ab) detected by a Rapid Anti-HCV test card® according to the manufacturer's procedure [9]. LC was diagnosed based on clinical and laboratory findings consistent with chronic liver disease as well as radiological evidence of LC by ultrasonography (US) [10, 11].

Patients were classified according to the CTP score and grading system into 3 groups: CTP A, CTP B and CTP C [2].

Anthropometric measurements

Body mass index (BMI)

Measurements of actual body weight (BW) and height for all patients were performed according to clinical standards, and (BMI) was calculated. Adjusted BW for peripheral lower limb edema and ascites was calculated according to the following equations [12].

$$\begin{aligned}\text{Adjusted BW} &= \text{Actual BW} - 1\ \text{kg}^{1}\\ &= \text{Actual BW} - 2.2\ \text{kg}^{2}\\ &= \text{Actual BW} - 6\ \text{kg}^{3}\\ &= \text{Actual BW} - 14\ \text{kg}^{4}\end{aligned}$$

1: For patients with peripheral lower limb eodema

2: For patients with mild ascites

3: For patients with moderate ascites

4: For patients with severe ascites

Muscle mass assessment of the upper and lower limbs

Circumferences were measured to the nearest millimeter using non stretch narrow tape. Mid-arm circumference (MAC) was measured at the midpoint between the tip of the acromion and olecranon process with the arm flexed at 90°. Tricuspid skin fold thickness (TSFT) was measured using a metal caliper. TSFT was then subtracted from MAC to determine the mid-arm muscle circumference (MAMC) according to the standard equation [MAMC (cm) = MAC (cm) − [3.14 × TSF (cm)] [13]. The cutoff point taken to diagnose low MAMC was < 24.5 cm for both males and females [14].

Mid-Calf circumference (MCC) was measured according to the protocol of the International Society for the Advancement of Kineanthropometry. Care was taken not to compress the subcutaneous tissue when placing the measuring tape around the calf and when measuring the calf circumference twice on each side where the circumference was the largest in the standing position; the average was calculated. An MCC of less than 34 cm and 33 cm for males and females, respectively, was taken as the cut-off for the diagnosis of low muscle mass [14].

Muscle strength assessment of the upper and lower limbs

Hand grip strength (HGS) was measured using a Jamar hand dynamometer (Sammons Preston Rolyan, IL, USA). Instructions and demonstrations were given to the patients according to the standard recommendations [15]. The measurements were performed by the same investigator who was blinded to the clinical data of the patients. For HGS, patients were instructed to grip the device for each hand as hard as possible 3 consecutive times. The maximum gripping value in kilograms (kg) was recorded and taken into analysis. An HGS under 26 and 18 kg for males and females, respectively, was the cutoff taken to diagnose low muscle strength of the upper limb according to the Journal of Society of Hepatology (JSH) criteria [16].

Lower leg extension strength (LES) isometric strength testing of maximal voluntary contraction of knee extensors was measured with increasing weights applied to ankle, with the subject seated in an adjustable straight-back chair, the lower leg unsupported and the knee flexed to 90°. The cutoff points were 18 kg and 16 kg for males and females, respectively [17].

The diagnosis of sarcopenia was based on the 2018 definition of sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP). "Probable sarcopenia" was diagnosed by decreased muscle strength as assessed using either HGS or (LES). However, "definitive sarcopenia" was diagnosed when there was decreased muscle strength in addition to altered muscle mass [18], as confirmed by anthropometry as either decreased MAMC or MCC below previously stated cutoff values.

Statistical analysis of data

Data were analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov–Smirnov test was used to verify the normality of the distribution of variables. Comparisons between groups for categorical variables were assessed using the chi-square test (χ^2), Monte Carlo. ANOVA *F* test (F) was used to compare the CTP groups. The Kruskal–Wallis test was used to compare different groups for abnormally distributed quantitative variables. Logistic regression was used to detect risk factors for CTP class C. The significance of the obtained results was judged at the 5% level.

Results

This study included 80 patients with HCV-induced LC were included. According to the CTP score and grading system, they were defined as A ($n=12$), B ($n=32$), and C ($n=36$). The characteristics of the study participants are summarized in Table 1.

Based on the EWGSOP criteria, 76% ($n=61$) of patients were diagnosed with "definitive sarcopenia" (Table 2), 19% ($n=15$) of patients had "probable sarcopenia", and 5% ($n=4$) of patients had "no sarcopenia". The characteristics of patients with definitive sarcopenia are described in Table 2.

In this study, definitive sarcopenia diagnosed by LES/MCC and HGS/MCC yielded a significant number of patients between the different CTP groups, being higher in grade C > B > A ($p=0.010$*). However, this difference was not found for definitive sarcopenia diagnosed by neither LES/MAMC nor HGS/MAMC. Moreover, no significant difference was found between the CTP groups regarding the total number of patients with definitive sarcopenia in each group.

For "probable sarcopenia", no significant difference was found between the different CTP groups when LES was taken as an indicator of muscle power. However, using HGS, there was a significant difference in the number of patients being highest in CTP C ($p=0.010$*). Moreover, the total number of patients diagnosed with "probable sarcopenia" varied significantly between CTP grades with CTP C being significantly higher than CTP B than A ($p=0.033$*), as shown in Table 3.

Determining the significance of the different anthropometric measures in discriminating CTP C from child A and B, LES/MCC and HGS/MCC significantly differentiated CTP C from CTP A and CTP B with diagnostic specificities of 88.64% and 86.36% and sensitivities of 36.11% and 41.67% for each anthropometric combination, respectively ($p<0.05$). However, this was not observed for the combined LES/MAMC ($p=0.960$) and HGS/MAMC as shown in Table 4.

Using multivariate logistic regression analysis, LES/MCC, and HGS/MCC were both found to be independent risk factors for the development of Child C cirrhosis ($p<0.05$), as shown in Table 5.

Patients diagnosed with definitive sarcopenia using LES/MCC and HGS/MCC had significantly lower serum albumin. However, no association was found with either the presence of HE, WBC count as shown in Table 6.

Discussion

The present study was conducted on a cohort of 80 Egyptian patients with HCV-induced liver cirrhosis who were further classified according to CTP score into grades A, B, and C in addition to anthropometric measures of muscle power and mass into "no sarcopenia", "probable sarcopenia" and "definitive sarcopenia". The prevalence of sarcopenia among the study population was 76% ($n=61$). It was found to be more prevalent in male patients than in females. This finding is in agreement with Carey et al. [19] and Montano et al. [20]. However, Endo et al. [21] found female sex to be an independent risk factor for the development of sarcopenia using CT with different cutoff

Table 1 Demographic, clinical, and laboratory characteristics of the study participants ($n=80$)

	Total ($n=80$)	CTP			Test of significance	P
		A ($n=12$)	B ($n=32$)	C ($n=36$)		
Gender						
Male	42 (52.5%)	7 (58.3%)	16 (50%)	19 (52.8%)	$\chi^2=0.245$	0.885
Female	38 (47.5%)	5 (41.7%)	16 (50%)	17 (47.2%)		
Age (years)						
Mean ± SD	56 ± 12.6	53.8 ± 8.4	57 ± 12.9	55.9 ± 13.7	$F=0.267$	0.766
Height (cm)						
Mean ± SD	170.2 ± 8	173.3 ± 6.9	170.5 ± 8	168.8 ± 8.3	$F=1.435$	0.244
Weight (kg)						
Mean ± SD	83.5 ± 15.4	95.9 ± 18.6	81.3 ± 11.8	81.2 ± 15.5	$F=5.120^*$	0.008^*
BMI (kg/m^2)						
Mean ± SD	30.7 ± 4.6	32.2 ± 6.1	29.5 ± 3.1	31.2 ± 4.9	$F=2.019$	0.140
HE						
Absent	45 (56.3%)	11 (91.7%)	21 (65.7%)	13 (36.1%)	$\chi^2=14.410^*$	$^{MC}p=0.004^*$
Grade 1 – 2	35 (43.8%)	1 (8.3%)	11 (34.4%)	23 (63.9%)		
Ascites						
Absent	14 (17.5%)	8 (66.7%)	6 (18.8%)	0 (0%)	$\chi^2=42.115^*$	$^{MC}p<0.001^*$
Tense	13 (16.3%)	0 (0%)	3 (9.4%)	10 (27.8%)		
Mild	13 (16.3%)	4 (33.3%)	7 (21.9%)	2 (5.6%)		
Moderate	39 (48.8%)	0 (0%)	16 (50%)	23 (63.9%)		
Massive	1 (1.3%)	0 (0%)	0 (0%)	1 (2.8%)		
LL edema	57 (71.3%)	2 (16.7%)	22 (68.8%)	33 (91.7%)	$\chi^2=24.877^*$	$<0.001^*$
Albumin					$F=15.771^*$	$<0.001^*$
Mean ± SD	2.6 ± 0.6	3.2 ± 0.4	2.7 ± 0.4	2.4 ± 0.5		
PA						
Mean ± SD	65.1 ± 17.3	71.1 ± 16.9	67.8 ± 16.4	60.7 ± 17.6	$F=2.371$	0.100
INR						
Mean ± SD	1.4 ± 0.3	1.3 ± 0.2	1.3 ± 0.2	1.5 ± 0.3	$F=3.390^*$	0.039^*
sCr						
Mean ± SD	1.2 ± 0.8	0.8 ± 0.4	1.2 ± 1	1.3 ± 0.7	$H=7.411^*$	0.025^*
WBCs						
Mean ± SD	7.4 ± 5.3	5.9 ± 5.3	6.8 ± 5.5	8.4 ± 5.2	$H=1.996\ 6.287^*$	0.043^*

BMI body mass index, *INR* international normalized ratio, *HE* hepatic encephalopathy, *sCr* serum creatinine, *PA* prothrombin activity, *WBCs* white blood cells, *SD* standard deviation, χ^2 chi-square, *F* ANOVA *F* test

* Values indicating a significant difference $p \leq 0.05$*

values for sarcopenia diagnosis. Recent studies have suggested that differences in skeletal muscle metabolism in female muscles are more capable of accumulating more lipids than males due to different hormonal characteristics, leading to more metabolic flexibility in females and a lower likelihood of developing sarcopenia [22].

In the current work, more than 90% of patients diagnosed with sarcopenia were either overweight or obese with a BMI of > 25 kg/m^2. This finding is in agreement with Isshi et al. [23] and Endo et al., who found BMI to positively correlate with low SMI. Patients with liver cirrhosis might have a condition of combined loss of muscle mass and a gain in adipose tissue, termed "sarcopenic obesity". Metabolic syndrome, in addition to a fat-rich, protein-poor diet as well as physical inactivity, leads to insulin resistance in addition to increased release of inflammatory adipokines, leading to muscle catabolism as well as obesity [24]. Furthermore, old-aged individuals tend to have more lipid stores in skeletal muscles. Since > 80% of study participants were over 50, in addition to the abovementioned factors, all may have contributed to the high prevalence of obesity in the studied group. BMI has long been considered one of the anthropometric measures for diagnosing sarcopenia. However, due to the high incidence of fluid retention as well as the high prevalence of sarcopenic obesity among patients

Table 2 Characteristics of patients with definitive sarcopenia

	No. (%)
CTP	
CTP A	9 (14.8%)
CTP B	24 (39.3%)
CTP C	28 (45.9%)
Age	
< 50	10 (16.4%)
≥ 50	51 (83.6%)
Mean ± SD	56.2 ± 12.5
Gender	
Male	37 (60.7%)
Female	24 (39.3%)
BMI (kg/m^2)	
< 25	3 (4.9%)
25–30	26 (42.6%)
> 30	32 (52.5%)
Mean ± SD	29.7 ± 3.5
HE	
Absent (history or absent)	35 (57.4%)
Present (grade 1 and 2)	26 (42.6%)
Serum albumin mean ± SD	2.6 ± 0.6
PA Mean ± SD	67.1 ± 15.6
WBCs Mean ± SD	7 ± 4.9
sCr Mean ± SD	1.2 ± 0.8

CTP Child–Pugh, *WBCs* white blood cells, *BMI* body mass index, *sCr* serum creatinine, *HE* hepatic encephalopathy, *SD* standard deviation

with liver cirrhosis, BMI was found to serve as a nonreliable measure.

There was a significant positive association between the number of patients diagnosed with "probable sarcopenia" who showed decreased muscle power and CTP grading being highest in grade C followed by B followed by A. However, regarding muscle mass, the diagnosis of "definitive sarcopenia" was not associated with CTP grade. Endo et al. and Hanai et al. [25] also stated that low skeletal muscle power was a stronger predictor of worse liver function and hepatic reserve than skeletal muscle mass. However, Hiraoka et al. [26] stated that low skeletal muscle mass using CT was correlated with poor patient outcome according to the CTP grade.

This current study evaluated the association of HGS, LES, MAMC, and MCC with the CTP grade of LC. The results showed a significant positive association between HGS and the degree of progression of LC according to the CTP grade. HGS is a universally well accepted method of validating muscle power when done using the standardized protocol [27] and cut-off points provided by the revised 2018 EWGSOP update, both of which were adopted in the present study [28].

LES may serve as a potential alternative for the assessment of sarcopenia and muscle power and to correlate positively to HGS [29]. Hence, the validity of LES for predicting the progression of liver disease was studied among this cohort of Egyptian patients with LC and a significant positive association was found between it and CTP grade being highest in CTP C. Both Bohannon et al. [30] and Alonso et al. [31] found a good correlation between HGS and LES for assessing muscle power. However, Felicio et al. [32] found no correlation between LES and HGS. This may be attributed to the lower BMI of the study participants and isokinetic assessment of LES rather than isometric.

Anthropometric measures have long been studied for the screening of sarcopenia. Jones et al., showed positive agreement between CT scans and MAMC for the prediction of sarcopenia in patients with colorectal cancer [33].

Table 3 Comparison and validity of anthropometrics among CTP groups ($n = 80$)

	Total ($n = 80$)	CTP			χ^2	*P*	Validity
		A ($n = 12$)	B ($n = 32$)	C ($n = 36$)			
Probable sarcopenia							
LES	61 (76%)	8 (66.7%)	24 (75%)	29 (81%)	1.005	0.605	
HGS	72 (90%)	10 (83.3%)	26 (81.3%)	36 (100%)	8.355*	$^{MC}p = 0.010$*	
Overall probable	76 (95%)	10 (83.3%)	30 (93.8%)	36 (100%)	5.022*	$^{MC}p = 0.033$*	
Definitive sarcopenia							
LES/MCC	51 (64%)	3 (25.0%)	18 (56.3%)	30 (83%)	14.550*	0.001*	0.001*
LES/MAMC	58 (73%)	9 (75%)	23 (71.9%)	26 (72%)	0.045	0.978	0.960
HGS/MCC	50 (63%)	1 (8.3%)	20 (62.5%)	29(81%)	20.030*	< 0.001*	0.003*
HGS/MAMC	55 (69%)	7 (58.3%)	21 (65.6%)	27 (75%)	1.406	0.495	0.275
Overall definitive	76 (95%)	10 (83%)	31 (96.9%)	35 (97%)	3.336	$^{MC}p = 0.198$	$^{FE}p = 0.623$

χ^2 chi-square test, *MC* Monte Carlo, *p* *p* value for comparing between CTP and different parameters, *FE* Fisher's exact test

* Statistically significant at $p \leq 0.05$

Table 4 Diagnostic sensitivity and specificity of anthropometric measures in diagnosing CTP C

	Total ($n=80$)	CTP		*p*	Sensitivity	Specificity	Accuracy
		A + B ($n=44$)	C ($n=36$)				
Definitive sarcopenia							
No	19 (23.8%)	11 (25%)	8 (22.2%)	0.771	77.78	25.0	48.75
Yes	61 (76.3%)	33 (75%)	28 (77.8%)				
LES/MCC							
No	62 (77.5%)	39 (88.6%)	23 (63.9%)	0.008*	36.11	88.64	65.0
Yes	18 (22.5%)	5 (11.4%)	13 (36.1%)				
LES/MAMC							
No	22 (27.5%)	12 (27.3%)	10 (27.8%)	0.960	72.22	27.27	47.50
Yes	58 (72.5%)	32 (72.7%)	26 (72.2%)				
HGS/MCC							
No	59 (73.8%)	38 (86.4%)	21 (58.3%)	0.005*	41.67	86.36	66.25
Yes	21 (26.3%)	6 (13.6%)	15 (41.7%)				
HGS/MAMC							
No	25 (31.3%)	16 (36.4%)	9 (25%)	0.275	75.0	36.36	53.75
Yes	55 (68.8%)	28 (63.6%)	27 (75%)				

*Statistically significant at ≤0.05

Table 5 Univariate and multivariate logistic regression analysis for the parameters affecting CTP grade C ($n=36$)

	Univariate		[a]Multivariate	
	p	OR (95%C.I)	*p*	OR (95% CI)
(LES/MCC)	0.002*	5.476 (1.902–15.766)	0.002*	6.645 (2.045–21.590)
(HGS/MCC)	0.004*	4.537 (1.644–12.526)	0.006*	4.418 (1.539–12.688)

OR odds ratio, *CI* confidence interval

* Statistically significant at $p \leq 0.05$

[a] Adjusted by gender and age and BMI and LES/MCC and HGS/MCC

Table 6 Relation between LES/MCC, HGS/MCC and HE, serum albumin, and WBC count

	Definitive sarcopenia			
	LES/MCC		HGS/MCC	
	No ($n=62$)	Yes ($n=18$)	No ($n=59$)	Yes ($n=21$)
HE				
Absent	36 (58.1%)	9 (50%)	36 (61%)	9 (42.9%)
Present	26 (41.9%)	9 (50%)	23 (39%)	12 (57.1%)
χ^2 (*p*)	0.369 (0.544)		2.075 (0.150)	
Serum albumin				
Mean ± SD	2.7 ± 0.6	2.4 ± 0.5	2.7 ± 0.6	2.4 ± 0.5
t (*p*)	2.238* (0.028*)		2.226* (0.029*)	
WBCs count				
Mean ± SD	7.1 ± 5.4	8.2 ± 5.3	6.8 ± 4.5	9 ± 7.1
U (*p*)	473.50 (0.330)		524.0 (0.296)	

HE hepatic encephalopathy, *WBCs* white blood cell count

*Statistically significant at ≤0.05

In addition, Alberino et al. showed MAMC and TSF to be independent prognostic risk factors for the outcome of LC [34]. In the present study, a positive, but nonsignificant, association was found between the frequency of sarcopenia diagnosed by combined HGS or LES with MAMC and CTP grade. The absence of a significant correlation between the current study and Alberino's study may be attributed to different cutoff values for diagnosing sarcopenia as well as differences in the etiology of liver disease. Additionally, taking into consideration that 95% of patients in the current study had a BMI > 25 kg/m^2 and that fat mass is known to affect the upper more than lower extremity circumferences [35], this might have weakened the association between MAMC and the prognosis of liver disease.

Additionally, combining either LES or HGS with MCC anthropometrics was found to be an independent sensitive diagnostic and prognostic biomarker of 'definitive sarcopenia'. MCC was found to be a good surrogate marker for determining sarcopenia in patients with LC according to Endo et al. [36] as well as Nishikawa et al. [37] In addition, MCC was regarded as the most sensitive anthropometric measure to diagnose sarcopenia among chronic liver disease patients by the World Health Organization (WHO) [38].

Thus, this study suggests that MCC reflects worse disease outcome and hence can more specifically and precisely predict liver disease progression. MAMC utilizes TSF for its calculation, which may not entirely and accurately reflect lipid metabolism dysregulations that occur as LC progresses [39].

Patients diagnosed with definitive sarcopenia using combined HGS/MCC or LES/MCC had significantly lower serum albumin than those with probable or no sarcopenia. Low serum albumin is known to reflect not only poor liver function but also poor nutritional status and low muscle volume. This finding is in agreement with Hiraoka et al. [40] as well as Endo et al. who both found low serum albumin to significantly correlate with low muscle power and mass.

No significant positive correlation was found between either HGS/MCC or LES/MCC and the presence of HE. Hyperammonemia is known to contribute to sarcopenia by interfering with muscle protein synthesis through myostatin activation, mitochondrial damage, and oxidative stress, leading to skeletal muscle autophagy [41]. In turn, sarcopenia is known to contribute to hyperammonemia, as ammonia clearance occurs primarily in skeletal muscle mitochondria in the case of liver cell failure, and hence, decreased skeletal muscle mass leads to hyperammonemia [42, 43]. Failure to demonstrate a significant association between the presence of HE and the presence of definitive sarcopenia in the current study may have two explanations. First, patients with grades 3 and 4 HE who mostly had severe hyperammonemia were excluded from the study due to technical difficulties in obtaining anthropometric measures from such patients. Second, not all HE cases are known to have hyperammonemia. Some HE patients with even grades 3 and 4 have normal ammonia levels; therefore, the presence of HE cannot be considered an accurate reflective measure of serum ammonia levels in patients with LC.

Translocation of gut flora in patients with LC is known to initiate influx of inflammatory cytokines as well as lipid-derived intermediates into the blood stream, leading to mitochondrial skeletal muscle damage and sarcopenia [44]. To date, the relationship between serum cytokines, WBC count and the presence of sarcopenia has not been thoroughly investigated. The current study showed no positive correlation between a high WBC count and sarcopenia diagnosis among the studied population.

This study has a few limitations. First, the patients recruited in the study were symptomatic cirrhotic patients with decompensated liver disease; however, asymptomatic LC patients with no reason for hospital admission were not included in the study. Second, this is a single-centered study, and variations in anthropometric measures owing to nutritional habits as well as labor and body built related to residence, whether urban or rural, have not been taken into consideration. Third, the application of different study population-based cutoff points may not consider population variances. Fourth, most patients enrolled in the study had sarcopenic obesity; hence, further studies are needed to validate the utility of the anthropometric measures among patients with a low BMI. Fifth, due to the cross-sectional nature of the study, further studies are needed to investigate the survival of patients in relation to anthropometric measures to augment the current study's findings.

Conclusions

Sarcopenia is a potential objective predictor of the outcome of patients with HCV-induced LC. Anthropometric measures for sarcopenia diagnosis, when performed using a standardized protocol and population-based cutoff points, can be used as objective biomarkers to monitor liver disease progression. Muscle power is a stronger predictor of a worse outcome of LC than low skeletal muscle mass. The combination of either HSG or LES with MCC serves as a potential promising noninvasive objective tool to monitor liver disease progression and hence opens the field for further research as to whether these tools could be validated in combination with CTP or MELD scoring systems for predicting outcome of liver disease.

Abbreviations

ALT	Alanine transaminase
F	ANOVA *F* test
AST	Aspartate transaminase
BMI	Body mass index
BW	Body weight
CBC	Complete blood picture
$\chi 2$	Chi square
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CSA	Cross-sectional area
CT	Computed tomography
CTP	Child–Pugh-Turcotte scoring system
DXA	Dual energy X ray absorptiometry
EWGSOP	European Working Group on Sarcopenia in Older People
FBG	Fasting blood glucose
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HE	Hepatic encephalopathy
HGS	Hand grip strength
INR	International normalized ratio
JSH	Japanese Society of Hepatology
kgs	Kilograms
LC	Liver cirrhosis
LC	Liver cirrhosis
LES	Lower leg extension strength
MAC	Mid-arm circumference
MAMC	Mid-arm muscle circumference
MCC	Mid-calf circumference
PA	Prothrombin activity
SD	Standard deviation
TSF	Tricuspid skin fold
US	Ultrasonography
WBCs	White blood cells

Acknowledgements

The authors present sincere gratitude to the staff of tropical medicine department for facilitating patients' data collection as well as clinical biochemistry department for providing the lab work, at Alexandria Faculty of Medicine.

Authors' contributions
ANA: clinical examination of recruited patients, reporting, writing, and revising the manuscript. HMA: anthropometric measurements, shared in writing and revising the manuscript. WIL: introducing idea of this research and manuscript writing. All authors read and approved the final manuscript.

Funding
The authors declare that no financial or material support was provided by any parties and that there are no equity interests, patent rights, or corporate affiliations for this work. Facilities for research are available in our department for all with no restrictions. No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate
This study has been approved by the Faculty of Medicine, Alexandria University Ethics Committee. The present work had been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The serial registration number for this study is 0305692. All patients had given an informed written consent stating the title, procedure and purpose of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 5 March 2023 Accepted: 12 June 2023
Published online: 22 June 2023

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