Salama *et al. Egyptian Liver Journal* (2023) 13:24
https://doi.org/10.1186/s43066-023-00261-z

Egyptian Liver Journal

ORIGINAL RESEARCH ARTICLE

Open Access

Evaluation of handgrip strength as a predictor of sarcopenia in patients with HCV-related cirrhosis

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Abstract

Background Sarcopenia, characterised by a loss of muscle strength, quantity/quality, and physical performance, is associated with increased mortality and poor clinical outcomes in patients with liver cirrhosis. The use of the currently accepted methods for estimating muscle mass, such as computed tomography, dual-energy X-ray absorptiometry, and bioelectrical impedance analysis, in routine clinical practice is restricted because of limited availability, radiation exposure, time consumption, or high cost. Therefore, an alternative, simple, safe, reproducible, and financially accessible method for the routine assessment of sarcopenia is needed. Hence, we aim to assess the utility of handgrip strength (HGS) in diagnosing sarcopenia in patients with HCV-related cirrhosis compared to appendicular skeletal muscle index assessed by dual-energy X-ray absorptiometry (DEXA-ASMI). A total of 64 participants older than 18 years were consecutively recruited. The subjects were divided into the following groups: Control group included 32 healthy control subjects, and the HCV-related liver cirrhosis group included 32 patients who were subdivided equally into two subgroups (Child A and Child C) with 16 patients each. All participants were subjected to dominant hand dynamometer and DEXA scan.

Results The prevalence of sarcopenia was significantly higher in the cirrhosis group than in the control group (7.75 ± 1.35 vs. 8.29 ± 1.25 kg/m^2, $P < 0.001$), with increasing prevalence in the Child C class group ($P < 0.001$). HGS was significantly lower in the Child C group compared to other groups ($P < 0.001$). Regarding the differentiation of sarcopenic patients, defining HGS using a cutoff of ≤ 28.6 kg has an AUC of 0.879, sensitivity of 100%, specificity of 66.7%, PPV of 61.1%, and NPV of 100% (95% *CI* = 0.715 to 0.967; $P < 0.0001$).

Conclusion Given the low cost, reproducibility, and safety of handgrip strength dynamometry, this is a promising method for both the diagnosis of sarcopenia as well as serial monitoring of muscle function in patients with HCV-related cirrhosis.

Keywords Sarcopenia, Cirrhosis, Handgrip strength, DEXA

Background

Sarcopenia is a malnutrition-associated syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength [1, 2]. The liver is the primary organ of nutrient metabolism of the human body; therefore, liver cirrhosis causes malnutrition and consequently

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results in secondary sarcopenia in 30–70% of cirrhotic patients, especially those with advanced disease [3, 4].

Cirrhotic patients with sarcopenia have impaired protein synthesis and accelerated skeletal muscle proteolysis through several mechanisms, including malnutrition, ethanol consumption, decreased hepatic protein synthesis, altered skeletal muscle proteostasis, gut microbiome dysbiosis, raised myostatin levels, hyperammonemia, and low testosterone and growth hormone levels [3, 5–10]. Furthermore, altered hepatic immune responses result in endotoxemia and systemic inflammation, which induce sarcopenia progression through mechanisms including IGF-1 and insulin suppression [11]. Finally, bile acid altered metabolism may incur excessive growth of intestinal bacteria, as well as reduce nutrient absorption, particularly fat-soluble vitamins such as vitamin D [12].

Sarcopenia represents a significant economic and social burden in patients with cirrhosis [13]. It is associated with higher rates of morbidity, especially falls, fractures, disability, hepatic encephalopathy, infections, and hospital admissions [1, 14–16]. Additionally, sarcopenia was found to be an independent predictor of impaired quality of life [17] and mortality [16, 18, 19]. Sarcopenia is also associated with poorer clinical outcomes after liver transplantation, such as ventilator support, higher incidence of postoperative sepsis, organ rejection, neurological complications, length of ICU and hospital stay, mortality, and lack of functional independence [20]. This highlights the importance of early diagnosis and prompt evaluation of underlying etiologic risk factors for developing a personalised management plan, as stated in the recent AASLD guidelines [1]. However, there is currently no standardised definition of sarcopenia related to liver disease [21]. Additionally, patients with cirrhosis have alterations in the hydration fraction and density of fat-free mass even in the early stages of disease. These fluid imbalances impair the performance of available methods for skeletal muscle evaluation [22, 23]. Under current conditions, the accurate diagnosis of sarcopenia in patients with cirrhosis often remains elusive, and a suitable method for skeletal muscle assessment that is not influenced by body fluid changes is clearly needed [24].

Generally, there are several definitions for the diagnosis of sarcopenia, but all include low skeletal muscle mass alone or combined with low muscle strength [2]. However, muscle strength tends to decline prior to muscle wasting and has been associated with adverse outcomes more consistently than low muscle mass [2]. Hence, more recent studies tend to focus on muscle strength rather than muscle mass to diagnose sarcopenia and predict clinical outcomes [25, 26]. In addition, the use of the currently accepted methods for estimating muscle mass, such as computed tomography, dual-energy X-ray absorptiometry (DEXA), and bioelectrical impedance analysis, in routine clinical practice is restricted because of limited availability, radiation exposure, time consumption, or high cost. Therefore, an alternative, simple, safe, reproducible, and financially accessible method for the routine assessment of sarcopenia is needed [2].

The measurement of handgrip strength (HGS) is a method to quantify muscle function and quality. It measures mainly the hand and forearm muscle strength, but it has significant correlations with the muscle strength in the lower limbs and many other parts. Consequently, HGS reflects the degree of muscle strength of the whole body [27]. Previous studies have demonstrated that HGS is an independent predictor for malnutrition and cirrhosis-related complications, such as refractory ascites, spontaneous bacterial peritonitis, variceal bleeding, hepatorenal syndrome, and mortality [26, 28–30].

Using HGS may be of great utility since it is simple, easily reproducible, non-invasive, low cost, sensitive to nutritional changes, and is performed at the patient's bedside or during outpatient clinics without additional risk [2]. Therefore, we aim to assess the utility of HGS in diagnosing sarcopenia in HCV-related chronic liver disease patients compared to appendicular skeletal muscle index assessed by dual-energy X-ray absorptiometry (DEXA-ASMI).

Methods

For this observational study, a total of 64 participants older than 18 years were consecutively recruited from the outpatient clinics of the Department of Internal Medicine, Ain Shams University Hospitals, Cairo, Egypt, from June 2020 to August 2022. The subjects were divided into the following groups:

i. Control group: The control group included 32 healthy control subjects who were matched with cirrhotic patients with regard to sex, age, and body mass index (BMI).
ii. The HCV-related liver cirrhosis group: This group included 32 patients who were subdivided equally into two subgroups comprising 16 subjects each (Child-Turcotte-Pugh A and C cirrhotic patients).

Patients were excluded if they had other causes of liver disease, alcohol abuse, coinfection with HIV or HBV, hepatic encephalopathy, hepatocellular carcinoma or other malignant tumours, active antiviral treatment, transjugular intrahepatic portosystemic shunt insertion, or liver transplantation. Other causes of exclusion include pregnancy; the presence of severe comorbidities such as respiratory failure, heart failure, and renal failure requiring dialysis; history of recent use of drugs affecting

psychometric performances; and existence of neurological, psychiatric disorders, or musculoskeletal disease or deformity that could interfere with the muscle mass or muscle strength evaluation [31].

Demographic and clinical data collection

All participants were subjected to clinical, laboratory, HGS, and DEXA exams. Anti-HCV and HCV-RNA were assessed using third-generation enzyme immunoassay (EIA; AxSYM HCV 3.0, Abbott Laboratories, Chicago, IL, USA) and an in-house direct reverse transcriptase polymerase chain reaction (RT-PCR) assay, respectively.

Cirrhosis diagnosis was based on clinical characteristics, histological criteria, laboratory data, or imaging exams [32]. Severity of liver disease was evaluated using the Child–Pugh score and the model for end-stage liver disease (MELD) score [33, 34]. Ascites grade was evaluated according to the principles of the International Club of Ascites [35].

Included individuals were subjected to the following evaluations:

Anthropometric assessment

- Body weight was assessed with each participant standing barefoot and wearing light clothes in the centre of a single electronic scale platform with an accuracy of 0.1 kg (BOD POD; Life Measurement Instruments, Concord, CA, USA).
- Height was measured using a single stadiometer accurate to 0.1 cm; participants stood barefoot with heels together, back straight, and arms extended at the side of the body.
- Body mass index (BMI) was calculated as the weight divided by the squared height (kg/m^2) and categorised according to the World Health Organization criteria [36].
- The waist circumference was determined midway between the lowest rib and the top of the iliac crest at the end of a normal expiration.
- The hip circumference was determined at a horizontal plane at the maximum extension of the buttocks.
- The waist/hip ratio (W/H) was calculated by dividing waist measurement by hip measurement. Healthy W/H is 0.9 or less in males and 0.85 or less in females.
- The mid-arm circumference (MAC) was measured by placing the tape at the midpoint between the tip of the acromion and the olecranon process with the subject sitting upright and their arm flexed at 90° toward the chest.
- The mid-arm muscle circumference (MAMC) was calculated using the MAC and the triceps skinfold thickness according to standard equations as previously mentioned [37]. The threshold used to define low skeletal muscle mass was < 10th percentile of the sex- and age-specific MAMC [38]. All measurements were taken using a 150 cm non-distensible tape with an accuracy of 0.1 cm [39].

Handgrip strength assessment

HGS was assessed using a digital hand dynamometer Camry device (CAMRY Digital Hand Dynamometer, Model: EH101). The participants held an ergonomic position to perform the test, sitting upright in a chair with a backrest but no armrests. The feet were maintained on the floor with 90° knee flexion. The arm was positioned with 90° elbow flexion and neutral forearm pronosupination [40]. The subjects received explanation of the dynamometer. A single blinded instructor encouraged participants to produce their maximal HGS with their dominant hand. The best result of three attempts with a 1-min pause between was documented in kilograms (kg). Reduced HGS was defined using the cutoffs of ≤ 26 kg in males and ≤ 18 kg in females [2].

Dual-energy X-ray absorptiometry (DEXA)

All scans were performed on a single Prodigy DEXA scanner (GE Lunar, Madison, WI, USA; GE part number: LU43616EN.Jan-2010) [41]. Participants removed all metal objects and were instructed to empty their bladders. They then laid in the supine position on the scanning table centre, with palms down and arms at the side of the body [42]. Measurements of segmental muscle mass (considering the muscle limbs only) were obtained from all participants and used to calculate the ASM (the sum of the lean mass of the four limbs). We then calculated the DEXA-ASMI using the equation ASM (kg)/height^2 (m) [37]. Depletion of skeletal muscle mass was identified according to the European Working Group on Sarcopenia in Older People (EWGSOP2) recommendations as $ASMI < 7.0$ kg/m^2 in males and $ASMI < 5.5$ kg/m^2 in females [2]. Additionally, DEXA examinations were performed on the lumbar spine and femoral neck. According to World Health Organization references, osteoporosis was described as a T score ≤ −2.5 and osteopenia as −2.5 < T score < −1 [43].

Ethical approval was given from the Faculty of Medicine, Ain Shams University Ethics Committee (approval number: MD 116/2017-FWA 000017585). This study was performed in accordance with the ethics principles of the Declaration of Helsinki. Written informed consent was obtained prior to participation.

Statistical analysis

Data were evaluated using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA). Numerical data were presented as mean and SD, and intergroup differences were compared using an unpaired *t*-test. Categorical data were presented as a ratio or as number and percentage, and differences were assessed using the Pearson chi-squared test or Fisher's exact test if appropriate. Ordinal data were assessed using the chi-squared test for trend. Correlation between numerical variables was analysed using the Pearson correlation. Associations between continuous and ordinal variables were assessed using the Kendall tau rank correlation. Associations between continuous and nominal variables were analysed using the point biserial correlation. Receiver-operating characteristic (ROC) curve analysis with estimation of Youden's index was used to assess the diagnostic value of HGS. Two-sided *P*-values < 0.05 were considered statistically significant.

Results

Our study was performed on 64 subjects; HCV-related liver cirrhosis group included 32 patients (22 males and 10 females) with a mean age of 58.5 ± 11.0 years. This group was subdivided into two subgroups (Child A and Child C) with 16 patients each. The control group comprised 32 healthy volunteers (20 males and 12 females) with a mean age of 59.3 ± 12.1 years (Table 1). Mild ascites were detected in 3 patients with Child C cirrhosis.

The prevalence of sarcopenia was significantly higher in the cirrhosis group than in the control group, with increasing prevalence in the Child C class group (Tables 1, 2, Fig. 1). A significant difference in the presence of bone disease between the control and HCV-related cirrhosis groups was detected. Additionally, bone disease was more prevalent in the Child C patients (Table 2, Fig. 2).

HGS was significantly lower in the Child C group compared to other groups (Table 3, Fig. 3). By analysing patients' characteristics, we determined that sarcopenic patients are older, with higher Child class and lower HGS (Table 4, Fig. 4). Additionally, HGS was an independent predictor of sarcopenia in patients with HCV-related cirrhosis ($P = 0.021$) after adjusting for age and Child class by multivariable binary logistic regression analysis (Table 5). HGS significantly correlated with DEXA-ASMI, sex, Child class, MAMC, MAC, haemoglobin, serum albumin, conjugated bilirubin, prothrombin time, prothrombin concentration, INR, and bone disease by DEXA scan (Table 6).

Regarding the differentiation of sarcopenic patients, defining HGS using a cutoff of ≤ 28.6 kg has an AUC of 0.879, sensitivity of 100%, specificity of 66.7%, PPV of 61.1%, and NPV of 100% (95% *CI* = 0.715 to 0.967; $P < 0.0001$) (Fig. 5).

Table 1 Characteristics of study participants

Variable	Cirrhosis group (*n* = 32)	Control group (*n* = 32)	*p*-value
Age (years)	58.5 ± 11.0	59.3 ± 12.1	0.783
BMI (kg/m^2)	25.5 ± 4.4	28.0 ± 7.9	0.400
Sex (F/M)	10/22	12/20	0.076
Total lean mass (kg)	60.25 ± 8.50	64 ± 6.72	0.021
Total fat mass (kg)	18.6 ± 3.25	21 ± 2.45	< 0.001
DEXA-ASMI kg/m^2	7.75 ± 1.35	8.29 ± 1.25	< 0.001

Discussion

Detecting sarcopenia in patients with cirrhosis can be challenging because the clinically available methods for skeletal muscle mass assessment are affected

Table 2 Prevalence of sarcopenia and bone disease in patients with HCV-related cirrhosis and control participants

	Cirrhosis group			Control group (*n* = 32)	*p*-value
	Total (*n* = 32)	Child A (*n* = 16)	Child C (*n* = 16)		
	n (%)	*n* (%)	*n* (%)	*n* (%)	
Sarcopenia					
No	21 (65.6%)	14 (87.5%)	7 (43.8%)	30 (93.8%)	< 0.001
Yes	11 (34.4%)	2 (12.5%)	9 (56.3%)	2 (6.3%)	
DEXA-BMD					
Normal	2 (6.3%)	2 (12.5%)	0 (0.0%)	13 (40.6%)	< 0.001
Osteopenia	18 (56.3%)	9 (56.3%)	9 (56.3%)	15 (46.9%)	
Osteoporosis	12 (37.5%)	5 (31.3%)	7 (43.8%)	4 (12.5%)	

Data are number (*n*) and percentage (%)

DEXA-BMD dual-energy X-ray absorptiometry bone mineral density

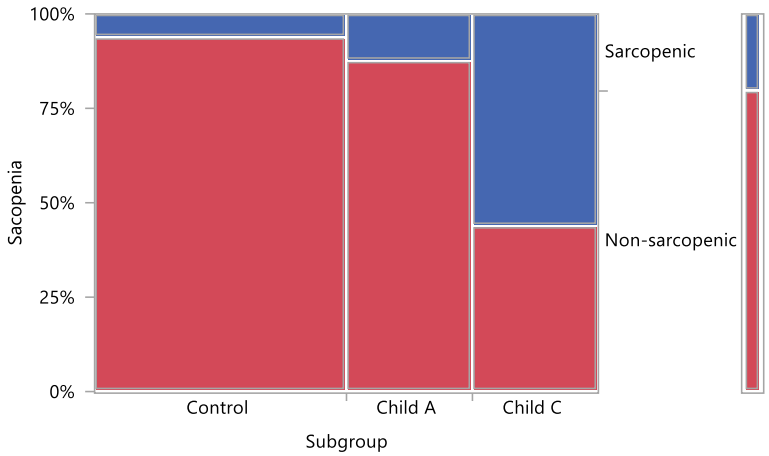

Fig. 1 Prevalence of sarcopenia in the control and cirrhosis groups

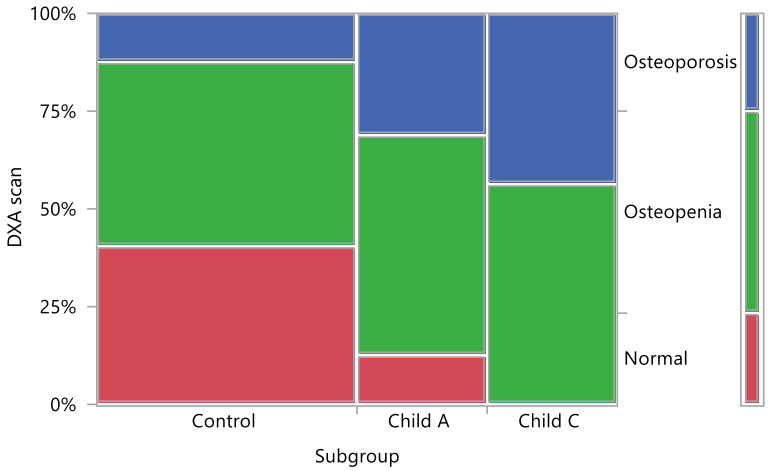

Fig. 2 Result of bone mineral density by DEXA scan in the control and cirrhosis groups

Table 3 Comparison of handgrip strength in the control and cirrhosis groups

Variable	Control ($n=32$)		Child A ($n=16$)		Child C ($n=16$)		*p*-value*
Handgrip strength (kg)	32.20 ± 8.38		35.96 ± 8.6		21.1 ± 5.9		$p>0.05$¶ <0.001§
	Male (22)	Female (12)	Male (12)	Female (4)	Male (10)	Female (6)	
	36.02 ± 7.98	25.83 ± 4.15	39.29 ± 6.67	26 ± 5.4	24.37 ± 4.50	15.76 ± 3.36	<0.001#

Data are mean ± SD

* One-way analysis of variance and Tukey's post hoc test

¶ *p*-value control versus Child A group

§ *p*-value control versus Child C and Child A versus Child C

p-value male patients versus female patients in all groups

strongly by the presence of ascites and peripheral oedema [44, 45]. This challenge can be partly overcome using a DEXA scan by focusing only on the ASMI [46]. Additionally, cirrhotic osteodystrophy is a common complication in cirrhotic patients; therefore, DEXA is frequently performed in these patients to assess BMD [47]. Therefore, DEXA body composition scans can be performed simultaneously with no added time or

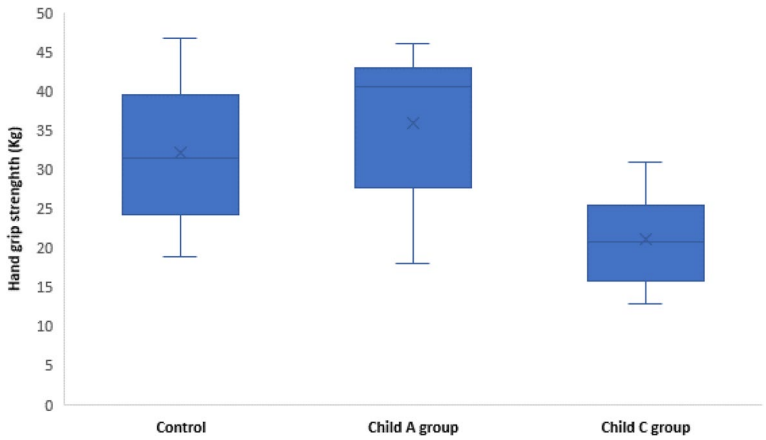

Fig. 3 Mean handgrip strength in the control and cirrhosis groups

radiation. Hence, DEXA-ASMI was recommended as a diagnostic tool for sarcopenia by the EWGSOP2 [2]. The DEXA scan is simple and safe but costly, which makes it unsuitable for serial assessment of sarcopenia in cirrhotic patients. Therefore, HGS represent an interesting and suitable method for this purpose.

In the present study, the prevalence of sarcopenia in cirrhotic patients equals 34.4%. Of note, the frequency of sarcopenia in patients with cirrhosis has varied widely among studies (ranging from 17 to 70%), fluctuating according to patient sex, severity of disease, and the criteria and method applied to diagnose this condition [41, 48].

Our result is similar to the studies of Sinclair et al. (31%) [49], Belarmino et al. (24%) [46], and Lindqvist et al. (39%) [50]. However, it was lower than previously reported, as Giusto et al. [41] published that HGS and the DEXA-ASMI detected sarcopenia in 46% of patients, and Eriksen et al. [51] reported low numbers as well (men: 49%, women: 43%). This may be attributed to the use of different cutoff values for sarcopenia [52]. Another likely explanation is the high percentage of patients with alcoholic liver disease in previous studies [46, 49, 51], since alcohol abuse causes skeletal muscle wasting independent of cirrhosis [53].

In accordance with the current study, Belarmino et al. obtained DEXA-ASMI and non-dependant HGS in 144 men with cirrhosis and found that muscle mass and strength were significantly lower in the cirrhosis group than in healthy participants (HGS, patients 25 ± 8.40 vs. control 39.69 ± 6.27 kg, $P < 0.001$, and DEXA-ASMI, 7.76 ± 1.45 vs. 9.29 ± 0.95 kg/m^2, $P < 0.001$) [46]. Subsequently, they further examined 124 male patients with cirrhosis, and 30% of them were diagnosed with low DEXA-ASMI (5.5 ± 2.1 kg/m^2) [54].

Another study included 231 males and 84 females with cirrhosis and 315 healthy matched controls. The aetiology of cirrhosis was alcohol in 76% of the patients and post-viral hepatitis in 9%. Low DEXA-ASMI was defined as *DEXA-ASMI* < 7.0 kg/m^2 in males and < 5.5 kg/m^2 in females. Low DEXA-ASMI was more prevalent in both males (49%) and females (43%) with cirrhosis compared with healthy males (8%) and females (5%; $P < 0.001$). The higher incidence of low DEXA-ASMI in cirrhosis corresponded to an odds ratio of 10.9 (3.2–37.3) in males and 15 (1.2–190) in females. In addition, DEXA-ASMI was lower in Child C compared with Child A and controls [51].

Other authors used a cutoff value of < 7.26 kg/m^2, and 30.9% of 420 cirrhotic men patients were classified as sarcopenic. Total DEXA-ASMI (kg/m^2) was 7.81 (7.06–8.59), sarcopenic = 6.43 (5.95–7.05), and non-sarcopenic = 8.09 (7.46–8.75), $P < 0.001$ [49].

In agreement with the current results, Santos et al. examined 129 subjects. More than half of the patients had hepatitis C. Mean lumbar spine T score was -1.51 ± 1.57, and mean femoral neck T score was -0.97 ± 1.13. Mean HGS was 25.97 ± 10.18 kg. For the lumbar spine, only low HGS was related to low T scores ($P = 0.0003$, 95% *CI* = 0.024–0.077). Of note, the variables related to liver function did not remain as significant. For the femoral neck, only age was correlated with low T scores. Once again, the other variables related to the liver disease severity did not remain significant. This result indicates that even in compensated cirrhosis, bone disease can already be present in the femoral neck of these patients [55].

Another study enrolled 300 subjects. The researchers excluded all patients with Child C cirrhosis and included patients of all aetiologies. Total HGS was 31

Table 4 Comparison of variables in HCV-related cirrhotic patients with and without sarcopenia

		Cirrhosis group ($n=32$)				*p*-value
		Non-sarcopenic ($n=21$)		Sarcopenic ($n=11$)		
Variable		***n***	**%**	***n***	**%**	
Sex	F	6	28.6%	4	36.4%	0.703
	M	15	71.4%	7	63.6%	
Child class	Child A	14	66.7%	2	18.2%	0.009
	Child C	7	33.3%	9	81.8%	
CRP	Negative	17	81.0%	8	72.7%	0.667
	Positive	4	19.0%	3	27.3%	
DEXA-BMD scan	Normal	2	9.5%	0	0.0%	0.326
	Osteopenia	12	57.1%	6	54.5%	
	Osteoporosis	7	33.3%	5	45.5%	
Age (years)		55.8	12.5	63.8	4.2	0.048
MELD score		9	4	10	6	0.630
BMI (kg/m^2)		25.0	4.8	26.4	3.7	0.426
MAMC (cm)		26.2	2.5	25.9	3.2	0.715
MAC (cm)		23.1	2.4	22.0	2.6	0.213
WC (cm)		92	16	100	10	0.116
HC (cm)		90.9	14.5	96.4	8.3	0.257
WHR		1.01	0.10	1.03	0.06	0.535
Haemoglobin (g/dl)		12.3	1.9	11.8	2.5	0.520
WBC (k/mm^3)		6.0	2.0	7.8	4.8	0.258
Platelets (k/mm^3)		150	68	158	76	0.752
Total protein (g/dl)		6.7	0.6	6.7	0.4	0.927
Serum albumin (g/dl)		3.83	0.74	3.54	0.52	0.257
AST (IU/l)		27.6	10.2	41.1	21.6	0.072
ALT (IU/l)		26	11	34	17	0.153
Total bilirubin (mg/dl)		0.69	0.30	0.98	0.67	0.098
Conjugated bilirubin (mg/dl)		0.24	0.11	0.35	0.22	0.155
PT (s)		12.84	0.90	13.27	1.41	0.300
PC (%)		89.9	9.9	87.5	12.9	0.550
INR		1.10	0.10	1.11	0.15	0.713
Serum creatinine (mg/dl)		1.09	0.36	1.17	0.43	0.609
Serum urea (mg/dl)		29.7	8.1	34.2	12.3	0.221
Serum Na^+ (mmol/l)		135.6	5.1	135.1	4.5	0.794
Serum K^+ (mmol/l)		4.01	0.67	4.54	0.81	0.056
Handgrip strength (kg)		33.7	10.0	19.7	5.8	< 0.001

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *CRP* C-reactive protein, *DEXA-BMD* dual-energy X-ray absorptiometry bone mineral density, *HC* hip circumference, *INR* international normalised ratio, *MAC* mid-arm circumference, *MAMC* mid-arm muscle circumference, *WBC* white blood cells, *WC* waist circumference, *WHR* waist-hip ratio, *PC* prothrombin concentration, *PT* prothrombin time

(22–39) kg. Compared to males, females had significantly lower HGS (22.8 ± 7.3 vs. 38.5 ± 12.4 kg, $P < 0.0001$) [56]. Other authors defined declined HGS as ≤ 26 kg in males and ≤ 18 kg in females. Of the 270 patients, decreased HGS was detected in 102 (38%). The median HGS was 29 kg in males and 17 kg in females [15].

In accordance with the present study, Sinclair et al. assessed 145 men using the sarcopenia cutoff for DEXA-ASMI of < 7.26 kg/m^2; finding the incidence of sarcopenia was 38.7% (46/119). The median DEXA-ASMI was 7.52 (6.87–8.36) kg/m^2. Using a cutoff value for HGS of < 30 kg, the incidence of sarcopenia was 45.9% (50/109). The median HGS was 30.9 (25–28) kg. Additionally, HGS was associated with DEXA-ASMI ($P < 0.001$) [26].

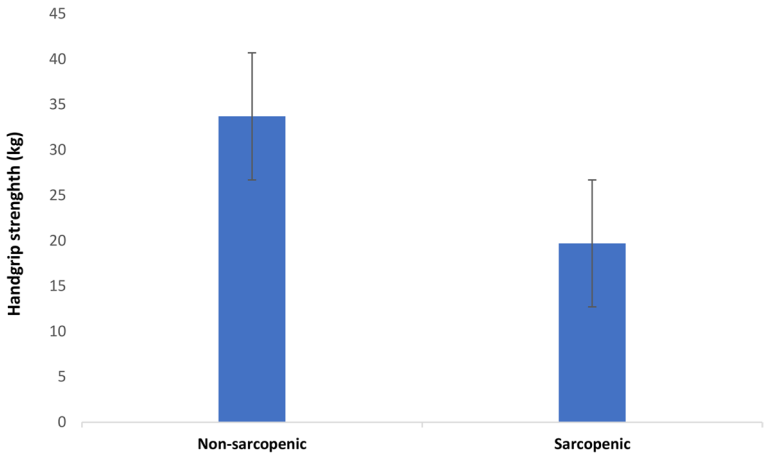

Fig. 4 Mean handgrip strength in patients with HCV-related cirrhosis with and without sarcopenia

Table 5 Multivariable binary logistic regression analysis for prediction of sarcopenia in patients with HCV-related cirrhosis

Variable	*B*	*SE*	*Wald*	*p-value*	*Odds ratio*	*95% CI*
Age (years)	0.089	0.091	0.949	0.330	1.093	0.914–1.307
Child C (=1)	−0.326	1.287	0.064	0.800	0.722	0.058–8.991
Handgrip strength (kg)	−0.212	0.092	5.319	0.021	0.809	0.675–0.969
Constant	−0.497	6.208	0.006	0.936		

B regression coefficient, *SE* standard error, Wald Wald chi-squared statistic, 95% *CI* 95% confidence interval

Ye et al. corroborated our results with a study that determined that HGS and DEXA-ASMI of patients were reduced compared to the control group ($P<0.05$). Moreover, HGS was associated with the Child–Pugh score ($P<0.05$). In addition, in comparing Child–Pugh A, B, and C groups with the control group, the investigators found that HGS decreased significantly along advanced Child class (Child A = 25.86 ± 9.39 kg, Child B = 23.36 ± 8.54 kg, Child C = 19.78 ± 9.57 kg, compared to control = 36.27 ± 11 kg, $P<0.001$) [57].

In partial agreement with the present study, a previous cross-sectional study that investigated 58 non-cirrhotic patients with chronic HCV hepatitis who were not under active pharmacological therapy. For nondominant HGS, 15 (57.7%) males and 22 (68.8%) females had HGS values below the 50th percentile. Additionally, HGS did not correlate with other clinical characteristics, such as age, gender, and liver fibrosis grade [58].

Another cross-sectional study included 80 patients with HCV-related cirrhosis and 80 control subjects. The authors compared HGS in patients against the control group using both the right hand (18.9 ± 4.8 vs. 41.9 ± 4.8 kg) and left hand (22.6 ± 3.7 vs. 29.6 ± 3.7 kg), $P<0.001$. They also compared the HGS in individuals with F0–F3 fibrosis against those with cirrhosis using the right (17.8 ± 3.7 vs. 16.8 ± 1.6 kg) and left hand (15.8 ± 2.4 vs. 14.2 ± 3.8 kg), $P<0.001$. Compared to control participants, patients with cirrhosis had significantly lower values of MAC (23.3 ± 2.6 vs. 28.1 ± 4.7 cm, $P<0.001$) and MAMC (18.9 ± 5.7 vs. 22.9 ± 4.2 mm, $P<0.001$). Additionally, HGS was significantly negatively correlated with the degree of liver fibrosis [59].

Similar to the present study, other investigators found that 15 of the 122 male patients with cirrhosis had lower HGS (19.57 vs. 30.55 kg, $P<0.001$) and albumin (3.10 vs. 3.75, $P=0.037$) than non-sarcopenic patients. Sarcopenia diagnosis was determined by considering *DEXA-ASMI* < 7.0 kg/m^2 and nondominant *HGS* < 27 kg [60].

Elucidating risk factors for the HGS loss in patients with cirrhosis seems clinically meaningful. Similar to our findings, researchers revealed significant associations between HGS loss with age, serum albumin, total bilirubin, prothrombin time-INR, and platelets count [61]. In agreement with the current findings, Hiraoka et al. described a significant correlation between serum albumin level and the HGS loss [62]. Additionally, Sung et al. reported that advanced age and sarcopenia were independent adverse predictors for skeletal muscle mass loss in 166 patients with cirrhosis [63]. In

Table 6 Relationship between handgrip strength and other variables

Variable	*Handgrip strength*	
	Coefficient of correlation/ association	***p*-value**
DEXA-ASMI	−0.624	< 0.001
Age	−0.335	0.061
Sex	0.563	0.001
MELD score	−0.249	0.170
Child class	−0.698	< 0.001
BMI	−0.195	0.285
MAMC	0.381	0.031
MAC	0.559	0.001
WC	−0.132	0.472
HC	−0.019	0.920
WHR	−0.176	0.335
Haemoglobin	0.549	0.001
WBC	−0.206	0.257
Platelets	0.327	0.067
CRP	−0.311	0.083
Total protein	0.304	0.097
Serum albumin	0.549	0.001
AST	−0.180	0.325
ALT	−0.039	0.833
Total bilirubin	−0.325	0.069
Conjugated bilirubin	−0.385	0.030
PT	−0.473	0.006
PC	0.527	0.002
INR	−0.465	0.007
Serum creatinine	−0.009	0.962
Serum urea	−0.098	0.592
Serum Na +	0.207	0.256
Serum K +	−0.208	0.253
DEXA-BMD scan	−0.304	0.037

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *CRP* C-reactive protein, *DEXA-ASMI* dual-energy X-ray absorptiometry appendicular skeletal muscle index, *DEXA-BMD* dual-energy X-ray absorptiometry bone mineral density, *HC* hip circumference, *INR* international normalised ratio, *MAC* mid-arm circumference, *MAMC* mid-arm muscle circumference, *WBC* white blood cells, *WC* waist circumference, *WHR* waist-hip ratio, *PC* prothrombin concentration, *PT* prothrombin time

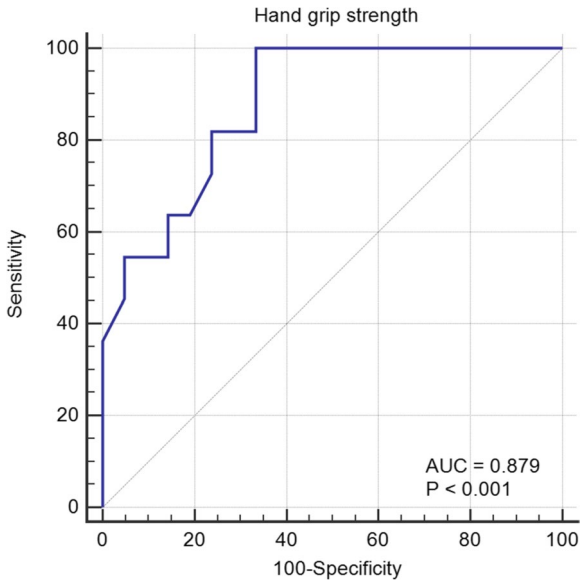

Fig. 5 Receiver-operating characteristic curve for discrimination between HCV-related cirrhosis patients with and without sarcopenia using the handgrip strength

contrast, sarcopenia and advanced age were not independent factors linked to the HGS loss in another study [61].

In agreement with the current results, in Luengpradidgun et al. study, 30 (16.5%) of the 146 patients had low HGS. The total mean HGS was 21.7 kg, in patients without sarcopenia = 31.3 kg, and in patients with sarcopenia = 16.7 kg ($P < 0.001$). Among 30 patients with sarcopenia, the median age was older, although not statistically significant, than non-sarcopenic patients. Likewise, platelets count and serum albumin in patients with sarcopenia were significantly lower than those without [64].

There are no standard cutoff values for diagnosing decreased HGS in patients with cirrhosis [50]. Of note, published cutoffs are based on heterogenous patient populations like those with different stages and aetiologies of liver disease [65] and those with cancer [66]. Therefore, a validated cutoff for sarcopenia diagnosis in HCV-related cirrhosis is of clinical interest. In the current study, we found that using a cutoff for HGS decline of ≤ 28.6 kg has a good predictive ability for sarcopenia. In an earlier report, HGS had an excellent diagnostic performance for detecting sarcopenia by using the Japan Society of Hepatology criteria (*HGS* < 26 kg for male, < 18 for female), where the sensitivity, specificity, NPV, and PPV were 88.2%, 100%, 98.7%, and 100%, respectively. Similarly, applying the European Working Group on Sarcopenia in Older People criteria (*HGS* < 30 kg for male, < 20 kg for female), the sensitivity, specificity, NPV, and PPV were 94.1%, 81.2%, 99.2%, and 82.5%, respectively [64].

This study is limited by small sample size. To the best of our knowledge, this is the first study to assess sarcopenia and HGS and its related factors among patients with HCV-related cirrhosis with the inclusion of Child C cirrhosis class. Early identification of sarcopenia would allow for prompt interventions to increase muscle mass and function, including nutritional supplementation [67], physical training [68], or medical therapy [69, 70], which will improve patients' prognosis [71].

Conclusions

Given the low cost, reproducibility, and safety of handgrip strength dynamometry, this is a promising method for both the diagnosis of sarcopenia as well as serial monitoring of muscle function in patients with HCV-related cirrhosis.

Abbreviations

BMI	Body mass index
DEXA-ASMI	Dual-energy X-ray absorptiometry appendicular skeletal muscle index
HCV	Hepatitis C virus
HSG	Handgrip strength
INR	International normalized ratio
MAC	Mid-arm circumference
MAMC	Mid-arm muscle circumference
MELD	Model for end-stage liver disease

Acknowledgements

Not applicable

Authors' contributions

MS, EB, MS, SA, and SS designed the study; AZ participated in the acquisition of data; MS, EB, MS, SA, SS, AZ, and GM participated in the analysis and interpretation of the data; MS, EB, MS, SA, SS, AZ, and GM revised the article critically for important intellectual content; and GM wrote the manuscript. The authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was given from the Faculty of Medicine, Ain Shams University Ethics Committee (approval number: MD 116/2017-FWA 000017585). This study was performed in accordance with the ethics principles of the Declaration of Helsinki. Written informed consent was obtained prior to participation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Received: 5 February 2023 Accepted: 6 May 2023
Published online: 15 May 2023

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