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Original article

Limited performance of subjective global assessment compared to computed tomography-determined sarcopenia in predicting adverse clinical outcomes in patients with cirrhosis

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SUMMARY

Background & aims: The subjective global assessment (SGA) is commonly used to assess nutritional status in patients with cirrhosis. Sarcopenia, a major component of malnutrition, is associated with survival in cirrhosis, and can be objectively diagnosed by computing the skeletal muscle index (SMI) using cross-sectional imaging. The aim of this study was to assess the prevalence of sarcopenia between SGA categories in patients with cirrhosis, and to determine their association with decompensation/mortality.
Methods: We included 315 patients (66% males) who were assessed for liver transplantation. All patients had SGA and SMI, and were evaluated for the presence of hepatic encephalopathy (HE) and ascites.
Results: Mean age was 54 ± 8 years. SGA categories were 126 SGA A (40%), 155 SGA B (49%), 34 SGA C (11%). Sarcopenia was present in 121 (38%) patients; of these, 82% were SGA A/B. Of SGA A patients, 25 (20%) had sarcopenia. There was a significant but only weak concordance between sarcopenia and SGA B/C ($\kappa = 0.28$, $p < 0.001$), and SGA C ($\kappa = 0.13$, $p < 0.001$). The latter was lost in overweight/obese patients. SGA B/C was associated with HE (OR 2.8, $p = 0.01$) and ascites (OR 2.3, $p = 0.002$). Median survival was shorter in patients with sarcopenia (20 [IQR 15.9–24.5] *vs.* 42 [IQR: 25.8–58.9] months, $p < 0.001$) and in SGA C patients (9.4 [IQR: 0–26.2] *vs.* 33 [IQR 20.2–45.7] months, $p = 0.01$). In univariate analysis both sarcopenia and SGA C were associated with mortality, but sarcopenia was the only factor that remained significant on multivariate analysis.
Conclusions: There was only a weak concordance between SGA and sarcopenia. This concordance was non-significant in patients who were overweight/obese. Sarcopenia was associated with mortality, whereas SGA was not. Sarcopenia by the SMI is a more efficient method to predict adverse outcomes in a timely fashion and has prognostic implications.

1. Introduction

Malnutrition is commonly seen in patients with cirrhosis, and has important prognostic implications, as it constitutes an independent predictor of mortality and is associated with decompensation and a poor quality of life [1]. Undernourishment in patients with cirrhosis is a potentially modifiable prognostic factor and ideally should be screened for by health providers. The original Child-Turcotte scale recognized the prognostic importance of nutritional status, but Pugh subsequently replaced it with the prothrombin time in 1973 [2].

The prevalence of malnutrition varies widely depending on the tools employed to perform the nutritional assessment and the stage of liver disease, being more common in patients with decompensated cirrhosis [3–5]. The subjective global assessment (SGA) is a popular method for evaluating nutritional status because it is simple, feasible at the bed-side, and economical [6]. Current nutrition guidelines recommend using the SGA and other simple bedside anthropometric methods to identify patients at risk of malnutrition [7,8]. Hence, some authors have considered SGA as the gold standard clinical tool with which other tools have to be compared [3,9,10]. However, there are several concerns with using

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Abbreviations

AILD	Autoimmune liver disease
BMI	Body mass index
CRP	C reactive protein
CT	Computed tomography
HCV	Hepatitis C virus
HE	Hepatic encephalopathy
HR	Hazard ratio
HU	Hounsfield units
INR	International normalized ratio
IQR	Interquartile range
L3	Third lumbar vertebra
LT	Liver transplantation
MELD	Model for end-stage liver disease
MELD-Na	MELD-Sodium
Na	Sodium
NASH	Non-alcoholic steatohepatitis
OR	Odds ratio
SD	Standard deviation
SGA	Subjective global assessment
SMI	Skeletal muscle index

the SGA as gold-standard. Most important, it includes weight change and the presence of edema as variables, whereas cirrhosis associated volume overload complicates the assessment of these variables [11]. In addition to this, the association between SGA and mortality has been inconsistent across studies with many of them failing to demonstrate a significant association after adjusting for the severity of liver disease [12–15]. On the other hand, sarcopenia is a consequence of chronic protein malnutrition, what has been shown to be a robust predictor of mortality in patients with cirrhosis [16,17]. Muscle wasting can be diagnosed by cross-sectional imaging by calculating the third lumbar vertebra skeletal muscle index (L3 SMI), which is currently considered the gold standard to detect sarcopenia in this population. This method has the advantage of being reproducible, accurate, objective, and not influenced by factors such as ascites [16,18]. However, the prevalence of sarcopenia between SGA categories has not been identified which was the first aim of this work. We also evaluated the contribution of sarcopenia by L3 SMI and nutritional status by SGA to mortality, and their association with hepatic encephalopathy (HE), ascites, and the presence of esophageal varices.

2. Materials and methods

2.1. Study population

In this retrospective study, eligible subjects were adult patients with cirrhosis who were seen in the liver unit of the University of Alberta Hospital for evaluation of liver transplantation (LT) between January 2000 and May 2013. We included 315 patients with SGA and computed tomography (CT) who had a diagnosis of cirrhosis by either histological, radiological (ultrasound or cross sectional imaging showing a lobulated liver and/or unequivocal signs of portal hypertension) or transient elastography (defined as liver stiffness >14 kPa) criteria.

2.2. Subjective global assessment

The SGA was performed by our registered dieticians at the time of LT assessment as recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) (8). The SGA rates patients in three categories: A – well nourished, B – mildly/moderately malnourished, and C – severely malnourished. It consists of 5 items from the medical history (dietary intake, weight change, gastrointestinal symptoms, functional capacity and the metabolic requirement of each person) and 3 items corresponding to the physical examination (loss of body fat, loss of muscle mass, and presence of edema/ascites).

2.3. Muscularity and sarcopenia assessment

CT scans used for muscularity analysis were performed as standard of care during LT assessment, but they did not constitute a mandatory part of our LT evaluation protocol. A transverse CT image from L3 in the inferior direction was assessed from each scan. Images were analyzed with SliceOmatic V4.3 software (Tomovision, Montreal, Quebec, Canada), which enables specific tissue demarcation by using previously reported Hounsfield unit (HU) thresholds. Skeletal muscle was identified and quantified by HU thresholds of -29 to $+150$. Muscles in the L3 region include psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal obliques, and rectus abdominis. Adipose tissue was identified by following HU thresholds: -190 to -30 for subcutaneous and -150 to -50 for visceral fat. Cross-sectional areas (cm^2) were automatically computed by summing tissue pixels and multiplying by pixel surface area. All CT images were analyzed by 2 trained observers. Cross-sectional area of muscle and adipose tissue was normalized for stature (cm^2/m^2). The L3 SMI was expressed as cross-sectional muscle area/height^2, and sarcopenia was defined according to the following cut-offs: L3 SMI: $<$ 39 cm^2/m^2 for women and $<$50 cm^2/m^2 for men [19]. Muscle attenuation indirectly measures fat infiltration in muscles. Mean muscle attenuation in HU was reported for the entire muscle area at the L3. To define myosteatosis, we used cutoff values that have been previously associated with mortality: <41 HU in patients with a BMI up to 24.9 kg/m^2, and <33 in those with a BMI $\geq$25 kg/m^2 [20,21].

2.4. Clinical and laboratory assessment

We collected the following information from each patient's chart: age, gender, etiology of cirrhosis, liver biochemistry tests and BMI. The biochemical parameters were obtained within 1 week from the index CT scan used to determine the L3 SMI. The BMI was computed from the estimated dry weight.

Presence of complications related to portal hypertension were operationally defined as follows:

- HE was considered when there was record of at least one hospital admission with the diagnosis of HE within the 12 months prior to the LT assessment and/or when patients were taking an HE treatment, specifically lactulose and/or rifaximin.
- Ascites was defined as present if patients were on diuretics, or if the index CT used to determine L3 SMI, or any previous imaging within the 12 months prior to the LT assessment, showed ascites.
- The presence of varices was based on endoscopic reports.

2.5. Statistical analyses

Data are presented as the mean ± standard deviation for normally distributed data, or frequencies and percentages. Normally-distributed numeric and categorical variables were compared with Student's t-test and chi squared test, respectively. Non-normally distributed variables were presented as median with the 25th-75th percentile range and were compared with the Mann–Whitney test. Patients in SGA B and SGA C categories were combined together as moderate-severe malnourished and the comparisons were made between patients with either severe (SGA C) or moderate-severe malnutrition (SGA B/C) and their counterparts. Concordance between sarcopenia and SGA, both in the whole sample and in a sub-analysis of overweight/obese patients, was evaluated using Cohen's kappa coefficient statistics; the correlation between L3 SMI and SGA was assessed using Pearson's rank correlation coefficient. Factors associated with decompensation events (HE, ascites) and the presence of varices were determined with logistic regression analysis. Survival analysis was performed with the Kaplan–Meier method, and resulting curves compared with the log-rank test. Survival was reported as median with interquartile range (IQR). To study the association between sarcopenia, SGA and mortality, we used the Cox proportional hazards model. In addition to this, in the patients that were listed for LT after the assessment ($n = 207$), we used a competing-risks regression model according to the method of Fine and Gray, considering transplant as the competing event. General, clinical, biochemical and body composition variables were all included in univariate analysis and variables with a p-value less than 0.1 in univariate analysis were included in multivariable regression analysis. Patients were followed from the date of the LT assessment until death, transplantation, or the last date of follow-up. Analyses were conducted using Stata version 12 (Stata Corp LP, College Station, TX, USA).

3. Results

3.1. Clinical and biochemical features of patients

Of the 315 patients, 209 (66%) were males. The mean age was 53.8 ± 8. The median survival and median follow-up time were 32.8 [IQR 20.8–44.8] and 10.9 [IQR 8.7–12.5] months, respectively. The most common etiology of cirrhosis was hepatitis C virus infection (122 patients, 39%) followed by non-alcoholic fatty liver disease (85 patients, 27%) and alcohol (68 patients, 22%). One hundred and thirty-one patients (42%) had a concomitant diagnosis of hepatocellular carcinoma. In terms of complications of portal hypertension, HE was documented in 66 patients (21%), ascites in 235 (75%) and esophageal varices in 266 (84%) (Table 1). Two hundred and seven patients (66%) were listed for LT after the assessment was completed.

Regarding the severity of liver disease, 42 (13%), 169 (54%), and 104 (33%) patients were Child-Pugh A, B, and C, respectively. The median for model for end stage liver disease (MELD) score was 14 (10–20).

Sarcopenia was present in 121 patients (38%). The SGA distribution was as follows: SGA A 126 patients (40%), SGA B 155 (49%) and SGA C 34 (11%). The median BMI was 27 (23–31) kg/m^2, with 189 patients (60%) being overweight or obese.

Those patients with sarcopenia and those classified as SGA B/C had significantly higher MELD scores, lower BMI, and higher frequency of HE and myosteatosis. Male gender and alcohol as the etiology of the cirrhosis were significantly more frequent in patients with sarcopenia and in patients assessed as SGA B/C (Tables 1 and 2).

3.2. Association between SGA and sarcopenia

Concordance was significant but weak between sarcopenia and malnutrition defined as SGA B/C ($k = 0.28$, $p < 0.001$), and almost null when considering only SGA C patients as malnourished ($k = 0.13$, $p < 0.001$). Likewise, the correlation between the L3 SMI and SGA was weak ($r = -0.25$, $p < 0.001$) (Fig. 1). Sarcopenic patients were more frequently classified as SGA B and SGA C when compared with non-sarcopenic patients (61 vs 42%, $p < 0.001$, and 18 vs 6%, $p < 0.001$, respectively). On the other hand, non-sarcopenic patients were more frequently classified as SGA A compared to sarcopenic patients (52 vs 21%, $p < 0.001$). Similarly, sarcopenia was significantly more frequent in patients with SGA C (65%) and SGA B (48%) than in SGA A patients (20%) ($p < 0.001$) (Tables 1 and 2). The median SMI was significantly higher in SGA A patients compared to SGA B/C ($p < 0.001$), with the lowest median SMI observed in SGA C patients ($p = 0.001$) (Table 2).

In a subanalysis of patients who were overweight or obese (BMI ≥ 25 kg/m^2), the concordance between sarcopenia and SGA B/C was again weak ($k = 0.3$, $p < 0.001$), with significance lost when considering only SGA C patients as malnourished ($k = 0.0$, $p = 0.5$). In the case of obese patients (BMI$\geq$30 kg/m^2) the concordance between sarcopenia and SGA B/C was almost null but significant ($k = 0.19$, $p = 0.02$) and non-significant in the case of SGA C patients ($k = -0.1$, $p = 0.8$).

3.3. Association between malnutrition and portal hypertension related complications

In the univariate analysis, sarcopenia [Odds ratio (OR) 2.9, $p < 0.001$], SGA C (OR 3.1, $p = 0.003$) and SGA B/C (OR 4.2, $p < 0.001$) were associated with HE (Table 3). In the multivariate analysis, after adjusting for MELD, sodium, alcohol induced cirrhosis and gender, SGA C was not significant (OR 2.0, $p = 0.11$), whereas SGA B/C (OR 2.8, $p = 0.01$) remained significant; sarcopenia was significant only in the model that included SGA C (OR 2.2, $p = 0.03$) but showed a trend toward significance in the model with SGA B/C (OR 1.9, $p = 0.07$). Regarding ascites, only SGA B/C was significant in the univariate (OR 2.8, $p < 0.001$) and multivariate analysis (OR 2.3, $p = 0.002$) after adjusting for MELD and sodium (Table 4). Finally, sarcopenia (OR 1.1, $p = 0.79$), SGA C (OR 1.1, $p = 0.88$) and SGA B/C (OR 1.2, $p = 0.45$) were not associated with the presence of esophageal varices.

3.4. Survival analysis in patients with malnutrition

Median survival was significantly shorter in patients with sarcopenia than in non-sarcopenic patients (20.2 [QR: 15.9–24.5] *vs*. 42.3 [IQR: 25.8–58.9] months, $p < 0.001$), and in patients with SGA C when compared to SGA A/B patients (9.4 [IQR: 0–26.2] *vs*. 33.0 [IQR: 20.2–45.7] months, $p = 0.02$) (Fig. 2a,b). In SGA A/B patients, median survival was shorter in sarcopenic patients when compared to non-sarcopenic patients (21.7 [QR: 17.0–26.3] *vs*. 42.3 [IQR: 24.5–60.1] months, $p = 0.002$). After stratifying the population by sarcopenia, survival time was only different between patients with SGA C when compared to SGA A/B in patients with sarcopenia (21.7 [QR: 17.0–26.3] *vs*. 3.9 [IQR: 0–8.7] months, $p = 0.02$), but not in non-sarcopenic patients (Fig. 3a,b). Finally, median survival was not significantly different between SGA A and SGA B/C patients (36.3 [IQR: 14.3–58.3] *vs*. 29.1 [IQR: 17.9–40.3] months, $p = 0.15$) (Table 5).

3.5. Association between malnutrition and mortality

In the univariate analysis using the Cox proportional hazards model, sarcopenia [Hazard ratio (HR) 2.1, $p < 0.001$] and SGA C (HR 1.9, $p = 0.02$), but not SGA B/C (HR 1.3, $p = 0.15$) were associated with mortality. In the multivariate analysis, after adjusting for MELD, BMI, sodium, ascites, and HE, sarcopenia remained significant (HR 1.6, $p = 0.04$) but not SGA C (HR 1.5, $p = 0.11$). The same

Table 1
Characteristics of patients with and without sarcopenia.

Characteristics	Total (n = 315)	Non-Sarcopenic (n = 194)	Sarcopenic (n = 121)	P-value
General				
Age, years	54 ± 8	53.7 ± 7.3	54.1 ± 9.1	0.65
Male	209 (66)	114 (59)	95 (79)	<0.001
Clinical				
Etiology				
NASH	85 (27)	59 (30)	26 (21)	0.08
HCV	122 (39)	78 (40)	43 (36)	0.48
Alcohol	68 (22)	29 (15)	39 (32)	<0.001
AILD	28 (9)	19 (10)	9 (7)	0.55
Other	12 (4)	8 (4)	4 (3)	0.77
Varices	266 (84)	163 (84)	103 (85)	0.87
Ascites	235 (75)	142 (73)	93 (77)	0.51
Hepatic encephalopathy	66 (21)	27 (14)	39 (32)	<0.001
Hepatocellular carcinoma	131 (42)	91 (47)	40 (33)	0.01
SGA				
SGA A	126 (40)	101 (52)	25 (21)	<0.001
SGA B	155 (49)	81 (42)	74 (61)	
SGA C	34 (11)	12 (6)	22 (18)	
Mortality during follow up	109 (35)	57 (29)	52 (43)	0.01
Liver transplantation	107 (34)	65 (33)	42 (35)	0.91
Biochemical[a]				
MELD	14 (10–20)	13 (10–17)	16 (12–23)	<0.001
MELD Na	17 (12–23)	14 (10–19)	20 (16–27)	<0.001
Bilirubin, umol/L	38 (23–84)	34 (21–62)	53 (26–122)	0.001
Creatinine, umol/L	75 (62–96)	73 (62–89)	85 (60–121)	0.005
Sodium, mmol/L	137 (134–140)	138 (135–140)	135 (132–139)	<0.001
INR	1.2 (1.3–1.6)	1.3 (1.2–1.6)	1.4 (1.2–1.8)	0.001
Ammonia, μmol/L	62 (39–92)	57 (37–88)	66 (45–100)	0.12
CRP, mg/L	6.7 (2.5–16.6)	5.7 (2.2–12.6)	10.1 (3.9–26.1)	0.002
Ferritin, μg/L	259 (93–611)	216 (70–485)	330 (116–754)	0.009
Body composition[a]				
BMI, kg/m^2	27 (23–31)	28 (24–32)	24 (21–27)	<0.001
Subcutaneous adipose tissue index, cm^2/m^2	46 (26–77)	61 (34–92)	29 (19–46)	<0.001
Visceral adipose tissue index, cm^2/m^2	28 (14–49)	33 (18–56)	21 (10–34)	<0.001
Myosteatosis	192 (61)	93 (48)	99 (82)	<0.001

NASH non-alcoholic steatohepatitis; HCV hepatitis C virus; AILD autoimmune liver disease; MELD model for end-stage liver disease; Na sodium; INR international normalized ratio; BMI body mass index; SGA subjective global assessment; CRP C reactive protein.
Numbers in parentheses are percentages.
Data are presented as mean ± SD (normally distributed variables)or median with 25th-75th percentile range (non-normally distributed variables).Normally-distributed numeric and categorical variables were compared with Student's t-test and chi squared test, respectively.
[a] Non-normally distributed variables were compared with the Mann–Whitney test.

results were obtained using the competing risks regression model in the 207 patients that were listed for LT (Table 6).

4. Discussion

In this study, we found that malnutrition determined by SGA (i.e. SGA B/C or SGA C) and sarcopenia have a significant, but only weak concordance. Both were associated with HE, only SGA was associated with ascites, and neither of them with esophageal varices. Importantly, survival was shorter in patients with sarcopenia and in patients categorized as SGA C; however, on multivariate analysis, only sarcopenia was an independent predictor of mortality. These findings suggest that the SGA was not as efficient as sarcopenia in predicting outcomes, the former being associated with complications related to portal hypertension such as HE and ascites, but not with mortality.

The weak concordance between malnutrition as per SGA and sarcopenia can be explained by the fact that 20% of patients who were considered to be SGA A (well-nourished) on clinical evaluation had sarcopenia, and likewise 21% of the patients with sarcopenia were considered SGA A. The finding of a weak association between SGA and sarcopenia is in agreement with a study by Sheean et al., where they found that the prevalence of sarcopenia was the same in normal and malnourished patients as per SGA in patients with respiratory failure. In their study, up to 60% of patients who had scores of SGA A were found to have sarcopenia with the highest rates of misclassification in obese patients. They concluded that one of the reasons for this was the fact that SGA was insensitive for the detection of malnutrition in obese patients [22]. Other authors have not found a significant difference between the SGA in patients with and without sarcopenia [17]. In keeping with this, we found that the concordance between malnutrition determined by SGA and sarcopenia was lower in overweight/obese patients, and it even turned to be non-significant when only considering SGA C patients.

The association between SGA B/C and baseline ascites is not surprising since the presence of ascites is assessed as part of the SGA's physical examination and this does not necessarily imply that SGA is a predictor of decompensation, but that the prevalence of malnutrition is higher in decompensated patients. Indeed, previous studies have not found a significant association between SGA and the incidence of decompensation events (HE, ascites) [23].

In terms of prognosis, SGA has shown discordant results regarding its association with mortality. This might be because SGA seems to be associated with the degree of decompensation and some studies have not adjusted this variable to see if the SGA is an independent predictor of mortality [14,24]. In our study, we did not find a significant association between SGA and mortality after adjusting for the presence of sarcopenia and the severity of liver disease, reinforcing previous findings from our group and a study

Table 2
Characteristics of patients according to SGA.

Characteristics	SGA A (n = 126)	SGA B (n = 155)	SGA C (n = 34)	SGA A *vs*. SGA B/C (p value)	SGA A/B *vs*. SGA C (p value)
General					
Age, years	53.8 ± 8	53.5 ± 8	55.6 ± 8	0.93	0.19
Male	75 (59)	113 (73)	21 (62)	0.04	0.55
Clinical					
Etiology					
NASH	35 (28)	45 (29)	5 (15)	0.80	0.09
HCV	56 (44)	53 (34)	12 (35)	0.07	0.69
Alcohol	14 (11)	42 (27)	12 (35)	<0.001	0.04
AILD	13 (10)	11 (7)	4 (12)	0.47	0.53
Other	7 (5)	4 (2)	1 (3)	0.19	0.78
Hepatocellular carcinoma	64 (51)	59 (38)	8 (24)	0.007	0.02
Varices	104 (82)	133 (86)	29 (85)	0.45	0.88
Ascites	79 (63)	129 (83)	27 (79)	<0.001	0.49
Hepatic encephalopathy	11 (9)	41 (26)	14 (41)	<0.001	0.002
Mortality during follow up	39 (31)	54 (34)	17 (50)	0.27	0.046
Liver transplantation	35 (28)	61 (39)	11 (32)	0.058	0.83
Biochemical[a]					
MELD	12 (9–17)	15 (11–20)	16 (12–23)	<0.001	0.07
MELD Na	13 (10–19)	18 (13–25)	20 (15–26)	<0.001	0.046
Bilirubin, μmol/L	30 (18–64)	46 (28–97)	43 (29–87)	<0.001	0.38
Creatinine, μmol/L	73 (61–87)	80 (62–105)	79 (62–120)	0.02	0.36
Sodium, mmol/L	138 (136–140)	136 (133–139)	136 (132–139)	<0.001	0.14
INR	1.2 (1.1–1.5)	1.4 (1.3–1.7)	1.4 (1.2–1.9)	<0.001	0.18
Ammonia, μmol/L	64 (39–84)	63 (40–97)	48 (28–83)	0.79	0.16
CRP, mg/L	4.4 (1.9–9.5)	7.9 (3.5–24)	13.0 (7.0–52.4)	<0.001	0.01
Ferritin, μg/L	192 (74–463)	286 (94–601)	486 (125–827)	0.053	0.048
Body Composition[a]					
BMI, kg/m^2	28 (25–32)	25 (23–29)	23 (20–28)	<0.001	0.001
Subcutaneous adipose tissue index, cm^2/m^2	65 (42–102)	34 (22–59)	23 (8–43)	<0.001	<0.001
Visceral adipose tissue index, cm^2/m^2	40 (19–61)	24 (14–39)	15 (5–28)	<0.001	<0.001
Skeletal muscle Index, cm^2/m^2	52 (45–57)	48 (42–55)	40 (37–52)	<0.001	0.001
Sarcopenia	25 (20)	74 (48)	22 (65)	<0.001	<0.001
Myosteatosis	66 (52)	99 (64)	27 (79)	0.01	0.02

NASH non-alcoholic steatohepatitis; HCV hepatitis C virus; AILD autoimmune liver disease; MELD model for end-stage liver disease; Na sodium; INR international normalized ratio; BMI body mass index; SGA subjective global assessment; CRP C reactive protein.
Numbers in parentheses are percentages.
Data are presented as mean ± SD (normally distributed variables) or median with 25th-75th percentile range (non-normally distributed variables).
Normally-distributed numeric and categorical variables were compared with Student's t-test and chi squared test, respectively.
[a] Non-normally distributed variables were compared with the Mann–Whitney test.

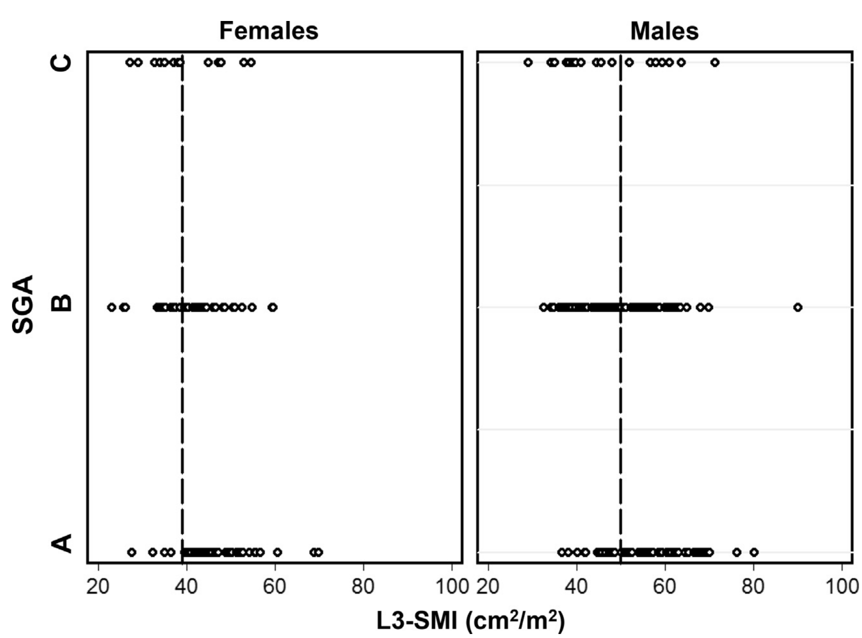

Fig. 1. Distribution of L3-SMI values according to SGA categories, by sex. Dispersion graphs depicting correlations between the L3 skeletal muscle index (L3 SMI) and subjective global assessment (SGA). The long-dash lines represent the cutoff that defines sarcopenia. L3-SMI = Third lumbar vertebra skeletal muscle index. SGA = Subjective global assessment.

Table 3
Association between sarcopenia and SGA with encephalopathy.

	Univariate			Multivariate[a]		
	OR	95% CI	P-value	OR	95% CI	P-value
Sarcopenia	2.9	1.6–5.1	<0.001	2.2[b]	1.1–4.3	0.03
				1.9[c]	0.9–3.8	0.07
SGA C	3.1	1.4–6.5	0.003	2.0	0.8–4.8	0.11
SGA B/C	4.2	2.1–8.4	<0.001	2.8	1.2–6.1	0.01

SGA Subjective global assessment; OR Odds ratio; 95% CI confidence interval.
ORs and P values were estimated using binary logistic regression.
[a] Adjusting for MELD, Na, alcohol related cirrhosis, and sex (Variables with a p-value <0.1 in univariate analysis).
[b] Model including sarcopenia and SGA C.
[c] Model including sarcopenia and SGA B/C.

Table 4
Association between sarcopenia and SGA with ascites.

	Univariate			Multivariate[a]		
	OR	95% CI	P-value	OR	95% CI	P-value
Sarcopenia	1.2	0.7–2.1	0.47	–	–	–
SGA C	1.3	0.5–3.2	0.50	–	–	–
SGA B/C	2.8	1.6–4.7	<0.001	2.3	1.3–4.0	0.002

SGA Subjective global assessment; OR Odds ratio; 95% CI confidence interval.
ORs and P values were estimated using binary logistic regression.
[a] Adjusting for MELD and Na (Variables with a p-value <0.1 in univariate analysis).

from Alvares da Silva and colleagues where there was no association between SGA and mortality [23,25]. In contrast, Castellanos-Fernandez and colleagues found a significant association between SGA and mortality. However, their analysis was only a bivariate analysis, and there was a strong concordance between malnutrition (SGA B/C) and decompensated cirrhosis (Child B/C). We speculate that in the case of multivariate analysis, adjusting for severity of liver disease, the association between the SGA and mortality would have been lost [26]. Huynh and colleagues also addressed this inconsistency, in the association between the SGA and mortality among the different studies. They consider that studies where the sample is mainly composed of decompensated patients, as their own, are prone to show a positive and significant association between the SGA and survival; on the other hand, they explain that studies enrolling mostly compensated patients usually fail to demonstrate this association [11]. This is in consonance with our findings where on subsequent analysis, when only considering sarcopenic patients, SGA C was independently associated with mortality, suggesting that SGA C may be capable of risk-stratifying sarcopenic patients to identify those who are severely ill and at imminent risk of dying (their median survival was only 3 months).

Identifying muscle wasting in cirrhotic patients is very important since sarcopenia has been shown to be an independent predictor of mortality [16]. In addition to this, it has been shown that the predictive value of sarcopenia is stronger in patients with a low MELD score (<15), where nutritional intervention probably are most useful [25]. The average MELD of the SGA A patients was 13.7, and 20% of them had sarcopenia, in other words, limiting the nutritional evaluation to the SGA would therefore preclude a timely intervention in almost one third of those patients benefitting most from an early diagnosis (*i.e.* patients with compensated cirrhosis).

The advantage of SGA is that it is inexpensive, widely available, and free of side effects for the patient. However, SGA has some elements which are subjective in nature and therefore compromise its objectivity and reproducibility. On the other hand, sarcopenia assessed by cross sectional imaging is a reproducible and objective method, which is widely available and gives important information not only about the quantity of muscle mass but also about its quality (i.e. myosteatosis). Moreover, with cross sectional image analysis additional parameters as subcutaneous and visceral adipose tissues can be obtained which are associated with important clinical outcomes in patients with end stage liver disease [21,27]. We recognize that assessing sarcopenia with a cross-sectional method is cumbersome and is associated with radiation exposure but many patients with cirrhosis will have CT scans of the abdomen for standard workup facilitating access to this objective sarcopenia assessment.

From our point of view, the rationale behind choosing a specific tool for assessing nutritional status in patients with cirrhosis should be to identify those at risk in a timely fashion in order to intervene early and to prevent further complications. In addition to this, the chosen method for assessing nutritional status should be associated with clinically relevant endpoints, such as mortality.

Our study has some limitations. Due to its retrospective nature, we were unable to simultaneously evaluate other nutritional assessment parameters such as hand grip strength, mid arm circumference, and bioelectrical impedance. As such, we could not evaluate previously proposed modifications of the SGA such as the Royal Free Hospital-Subjective Global Assessment (RFH-SGA) which adds mid-arm muscle circumference (MAMC) as an

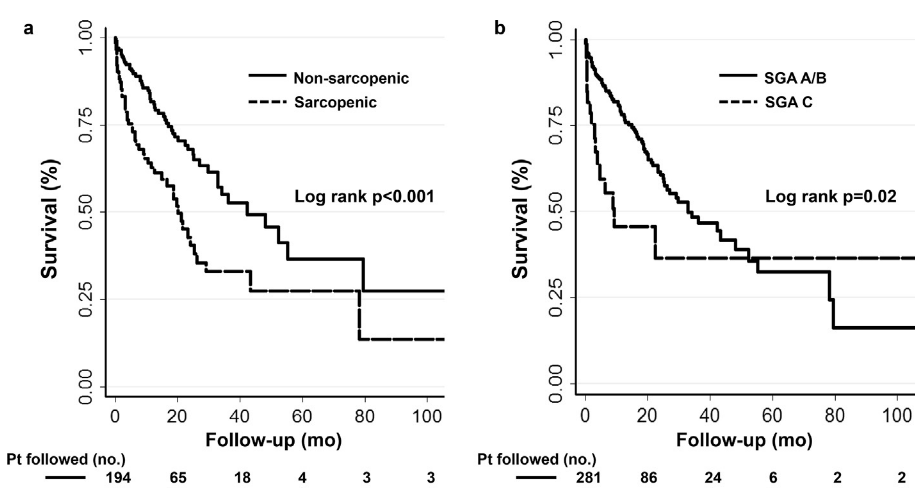

Fig. 2. Survival estimates by sarcopenia and SGA-C. The graphs show survival estimates by the Kaplan–Meier method. Figure 2a compares survival of patients with and without sarcopenia. Figure 2b compares survival of SGA A/B patients with that of SGA C patients. SGA = Subjective global assessment.

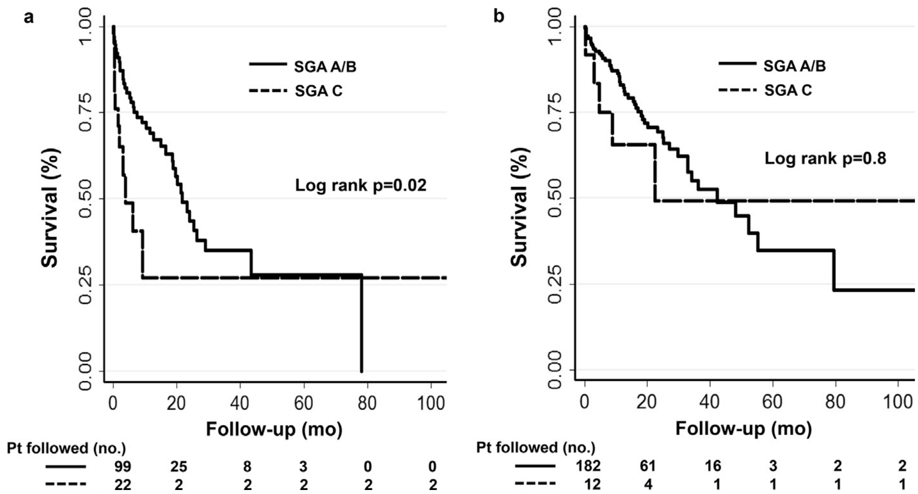

Fig. 3. Survival estimates by SGA-C, stratified by sarcopenia. The graphs show survival estimates by the Kaplan–Meier method. Figure 3a compares survival of SGA A/B with that of SGA C in patients with sarcopenia. Figure 3b compares the survival in non-sarcopenic patients. SGA = Subjective global assessment.

Table 5
Median follow up and survival times by sarcopenia presence and SGA categories.

	Median follow up, months (IQR)	Median survival, months (IQR)	P-value[a]
Total	10.9 (8.7–12.5)	32.8 (20.8–44.8)	–
Sarcopenia	5.9 (3.7–9.7)	20.2 (15.9–24.5)	<0.001
No sarcopenia	12.6 (11–15.6)	42.3 (25.8–58.9)	
SGA C	3.5 (2.0–8.9)	9.4 (0.0–26.2)	0.02
SGA A/B	11.7 (9.3–12.8)	33 (20.2–45.7)	
SGA B/C	9.2 (6.4–11.8)	29.1 (17.9–40.3)	0.15
SGA A	12.5 (9.1–16.2)	36.3 (14.3–58.3)	

SGA Subjective global assessment.
[a] Log rank test.

Table 6
Association between sarcopenia and SGA with mortality.

Cox proportional hazards model	Univariate			Multivariate[a]		
	HR	95% CI	P-value	HR	95% CI	P-value
Sarcopenia	2.1	1.4–3.1	<0.001	1.6	1.02–2.5	0.04
SGA C	1.9	1.1–3.2	0.02	1.5	0.8–2.7	0.11
SGA B/C	1.3	0.9–2.0	0.15	–	–	–
Competing risks regression model*	Univariate			Multivariate[b]		
	sHR	95% CI	P-value	sHR	95% CI	P-value
Sarcopenia	1.9	1.1–3.1	0.01	2.0	1.1–3.7	0.03
SGA C	2.4	1.1–4.8	0.02	2.1	1.0–4.6	0.06
SGA B/C	1.1	0.6–1.7	0.82	–	–	–

CI Confidence interval; SGA Subjective global assessment; HR hazard ratio; sHR subdistribution hazard ratio.
*HRs and P values were estimated using Fine–Gray subdistribution hazard model.
[a] Adjusting for BMI, ascites, MELD, Na and encephalopathy (Variables with a p-value <0.1 in univariate analysis).
[b] Adjusting for BMI and MELD (Variables with a p-value <0.1 in univariate analysis).

anthropometric parameter to the SGA, and has been shown to be independently associated with mortality [28,29]. However, the impact of MAMC in this setting is questionable as previous studies in patients with cirrhosis showed only a weak correlation between MAMC and CT-determined skeletal muscle mass [30,31], compromising its performance to detect malnutrition [13]. Finally, this study included only patients that had been referred for LT assessment, which may introduce a potential selection bias.

In conclusion, our study shows that the concordance between sarcopenia assessed by L3SMI and malnutrition as determined by SGA is weak. This was especially true for overweight/obese patients, where no significant concordance was found. Furthermore, sarcopenia but not SGA was independently associated with the mortality, which is a clinically significant endpoint amenable to be prevented with a timely nutritional intervention. Overall, these findings suggest that the SGA has a limited role in the assessment of patients with cirrhosis, but that it could be used as a risk stratifying tool to identify a particular group of sarcopenic patients at the highest risk of short term mortality.

Statement of authorship

Carlos Moctezuma-Velazquez conducted data analysis and drafted the paper; Maryam Ebadi assisted with the study conception, compilation of data and writing of manuscript; Rahima A. Bhanji and Guido Stirnimann assisted with the compilation and analysis of the data, revising the manuscript; Puneeta Tandon, and Aldo J. Montano-Loza contributed to interpretation of data and revising the manuscript. All authors have commented on the manuscript and approved the final version.

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Conflict of interest

The authors declare they do not have any conflict of interest.

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