Research article

Muscle mass dynamics is independently associated with long-term liver-related mortality in patients with cirrhosis

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ABSTRACT

Objectives: Sarcopenia has a detrimental impact on the prognosis of individuals with liver cirrhosis, however, the clinical significance of alterations in muscle mass remains uncertain. This study aims to investigate the influence of loss of skeletal muscle mass (LSMM) on the prognostic outcomes among patients diagnosed with cirrhosis.
Methods: In this retrospective analysis, a total of 158 individuals with cirrhosis who visited our hospital during the period from January 2018 to August 2023 were included. Computed tomography was utilized to measure the cross-sectional area of the skeletal muscles at the level of the third lumbar vertebra. This measurement enabled the determination of the skeletal muscle index for the purpose of diagnosing sarcopenia. The annual relative change in skeletal muscle area ($\Delta SMA/y$) was calculated for each patient, and LSMM was defined as $\Delta SMA/y < 0$. To assess the risk factors associated with liver-related mortality, a competing risk model was applied.
Results: Of the 158 cirrhotic patients, 95 (60.1 %) patients were identified as LSMM. The median of $\Delta SMA/y\%$ was -0.9 (interquartile range [IQR], -3.8, 1.6) in all patients. Chronic kidney disease (CKD) was confirmed as a risk factor of LSMM. During a median follow-up period of 68.1 (IQR, 43.5, 105.0) months, 57 patients (36.1 %) died due to the liver-related diseases. The competing risk model found that LSMM was significantly associated with liver-related mortality in cirrhotic patients (hazard ratio [HR], 1.86; 95 % CI, 1.01–3.44, $p = 0.047$). Cumulative survival was significantly higher in patients without LSMM than in those with LSMM ($p = 0.004$). Survival rates at 1-, 3-, and 5-years were 96.8 %, 81.0 %, and 65.1 %, respectively, in patients without LSMM, and 97.9 %, 80.0 %, and 56.8 %, respectively, in patients with LSMM.

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Conclusion: The utilization of LSMM can be valuable in the prediction of liver-related mortality among individuals diagnosed with liver cirrhosis. Paying attention to the management of skeletal muscle might play a role in enhancing the prognosis of patients with cirrhosis.

Clinical relevance statement: This study provides an additional indicator—LSMM for clinicians to help predict the liver-related mortality in patients diagnosed with cirrhosis.

Key points

The loss of skeletal muscle mass (LSMM) due to chronic liver diseases is the most frequent complication of liver cirrhosis.

The impact of LSMM on cirrhotic patients remains uncertain.

LSMM has great value in the prediction of liver-related mortality among individuals diagnosed with liver cirrhosis.

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1. Introduction

Liver cirrhosis, resulting from diverse injurious factors, manifests as a chronic liver ailment linked to persistent impairment of liver function and an altered hepatic structure [1,2]. It was associated with 2.4 % of global deaths in 2019, served as a leading cause of death worldwide [3]. Given its significant morbidity and the lack of efficacious therapeutic approaches, liver cirrhosis continues to rank among the primary global causes of mortality and morbidity, posing a significant burden on patients and the whole society [4]. Therefore, accurately determining the adverse prognostic factors to establish suitable treatment plans and enhance the outcomes of individuals with cirrhosis is of great importance.

Sarcopenia is a degenerative and widespread musculoskeletal condition characterized by the rapid depletion of muscle mass and functionality, leading to heightened negative consequences such as falls, diminished functionality, frailty, and mortality [5–7]. Additionally, it is linked to the development of infections, ascites, encephalopathy, and portal hypertension [6,8,9]. The occurrence of sarcopenia in cirrhosis ranges between 40 % and 70 %, which is subject to variation based on the population under evaluation, the assessment techniques employed, and the operational definitions utilized [8,10,11]. Moreover, individuals diagnosed with sarcopenia experienced more unfavorable outcomes following liver transplantation compared to those without this condition [12]. Additionally, the presence of sarcopenia is linked to increased mortality rates among cirrhotic patients, irrespective of liver function indicators like Child-Pugh (CP) score and end-stage liver disease (MELD) score [13,14]. These findings strongly suggest that it is imperative to assess not only liver function but also diagnose sarcopenia in order to effectively manage patients diagnosed with cirrhosis.

Chronic liver diseases often lead to the loss of skeletal muscle mass (LSMM), making it the most prevalent complication associated with liver cirrhosis [6,15]. The occurrence of LSMM, referred to as cachexia, is attributed to the gradual decline in anabolism and an increase in catabolism in severe chronic liver diseases. In patients diagnosed with hepatocellular carcinoma (HCC) or nonalcoholic fatty liver disease (NAFLD), this condition has been linked to a higher risk of all-cause mortality [16–18]. Nowadays, interest in sarcopenia in patients with liver cirrhosis has increased, however, the impact of LSMM on cirrhotic individuals, in addition to the presence of sarcopenia is still not fully understood. This retrospective research sought to examine whether changes in skeletal muscle can serve as a predictive factor for the prognosis of cirrhotic patients.

2. Methods

2.1. Study population

This retrospective study was carried out at Peking University People's Hospital between January 2018 and August 2023. We included patients with diagnoses of cirrhosis with the International Classification of Diseases, 10th revision, Clinical Modification (ICD-10-CM) codes K74.100 and K74.607. The inclusion criteria consisted of the following: a) patients aged 18 years or older; b) availability of complete patients' information; c) patients' two computed tomography (CT) imagines at the third lumbar vertebra were obtained and available to analyze; d) follow-up period >2 years from the baseline CT scan. Patients were excluded from the study if they met any of the following exclusion criteria: a) patients without a second CT performed >6 months after the baseline CT; b) patients with liver transplantation, incurable malignancy other than HCC, severe chronic respiratory or heart disease, nephrotic syndrome. Patients with a history of hepatocellular carcinoma were included if they did not show a current tumor on ultrasound or CT. The research protocol was approved by the Ethics Committee of Peking University People's Hospital (No. 2023PHB214-001) and carried out in accordance with the principles outlined in the 1975 Declaration of Helsinki and its 1983 revision. As the study is a retrospective study, informed consent was waived.

2.2. Clinical data collection and definitions

We extracted patients' hospitalization information from the electronic medical records of our hospital. The following patients'

characteristics were collected: age, sex, body mass index (BMI), underlying liver disease (alcohol-related or non-alcohol-related), co-morbidities (hypertension, diabetes, chronic kidney disease [CKD]), complications (HCC, ascites, variceal bleeding, spontaneous bacterial peritonitis [SBP] and hepatic encephalopathy [HE]). Laboratory parameters (thrombocyte, alanine aminotransferase [ALT] and MELD score) were also collected. Elevated ALT level was defined as ALT> 30 U/L in men or >19 U/L in women. MELD score was calculated with a standard formula: MELD = $3.78 \times \log$ [serum bilirubin (mg/dL)] + $11.2 \times \log$ [international standardized ratio] + $9.57 \times \log$ [serum creatinine] + 6.43 [19]. The interval from the clinical data to the baseline CT scan < ± 3 months.

2.3. Analysis of CT imaging parameters

The CT scans were conducted using the Philips 256-slice iCT scanner from Holland, GE Lightspeed VCT 64, and GE revolution 256 layers from the USA. A skilled radiologist, who had no knowledge of the clinical information, analyzed the CT images using SliceO-matic V5.0 software (Tomovision, Montreal, Canada). Tissue classification was determined based on Hounsfield units (HU) thresholds: -29 to 150 HU for the skeletal muscle area (SMA) at the level of the third lumbar vertebra, including the psoas, quadratus lumborum,

Table 1
Baseline characteristics of patients with liver cirrhosis (n = 158).

Variables	Total (n = 158)	Male (n = 96)	Female (n = 62)	*p* valve
Age (years)	57.1 ± 12.6	54.4 ± 12.8	61.4 ± 11.0	<0.001
<60	85 (53.8)	61 (63.5)	24 (38.7)	0.002
≥60	73 (46.2)	35 (36.5)	38 (61.3)	
BMI (kg/m^2)	23.2 ± 3.7	23.2 ± 3.4	23.2 ± 4.2	0.976
<28	143 (90.5)	89 (92.7)	54 (87.1)	0.240
≥28	15 (9.5)	7 (7.3)	8 (12.9)	
Alcoholic cirrhosis				<0.001
No	104 (65.8)	43 (44.8)	61 (98.4)	
Yes	54 (34.2)	53 (55.2)	1 (1.6)	
Co-morbidities (n, %)				
Hypertension				0.213
No	106 (67.1)	68 (70.8)	38 (61.3)	
Yes	52 (32.9)	28 (29.2)	24 (38.7)	
Diabetes				0.733
No	112 (70.9)	69 (71.9)	43 (69.4)	
Yes	46 (29.1)	27 (28.1)	19 (30.6)	
Chronic kidney disease				0.128
No	146 (92.4)	86 (89.6)	60 (96.8)	
Yes	12 (7.6)	10 (10.4)	2 (3.2)	
Laboratory parameters (n, %)				
Thrombocyte ($\times 10^9$/L)	102.7 ± 60.4	104.2 ± 61.3	100.4 ± 59.2	0.702
ALT (IU/L)	26.0 (19.0, 42.8)	25.5 (19.0, 44.0)	26.0 (18.5, 38.0)	0.516
< ULN	70 (44.3)	54 (56.2)	16 (25.8)	<0.001
≥ ULN	88 (55.7)	42 (43.8)	46 (74.2)	
MELD score	9.5 ± 4.6	9.0 ± 5.0	10.4 ± 3.9	0.055
Complications (n, %)				
Hepatocellular carcinoma				0.267
No	120 (75.9)	70 (72.9)	50 (80.6)	
Yes	38 (24.1)	26 (27.1)	12 (19.4)	
Ascites				0.155
No	63 (39.9)	34 (35.4)	29 (46.8)	
Yes	95 (60.1)	62 (64.6)	33 (53.2)	
Variceal bleeding				0.484
No	149 (94.3)	89 (92.7)	60 (96.8)	
Yes	9 (5.7)	7 (7.3)	2 (3.2)	
Spontaneous bacterial peritonitis				0.029
No	136 (86.1)	78 (81.2)	58 (93.5)	
Yes	22 (13.9)	18 (18.8)	4 (6.5)	
Hepatic encephalopathy				0.633
No	127 (80.4)	76 (79.2)	51 (82.3)	
Yes	31 (19.6)	20 (20.8)	11 (17.7)	
Radiographic analysis				
L3 SMA (cm^2)	116.8 ± 30.1	130.6 ± 29.2	95.4 ± 15.2	<0.001
L3 SMI (cm^2/m^2)	41.4 ± 8.6	44.1 ± 9.2	37.1 ± 5.3	<0.001
ΔSMA/y (%)	−0.9 (−3.8, 1.6)	−1.1 (−4.6, 2.4)	−0.6 (−2.6, 0.5)	0.861
Sarcopenia				0.038
No	85 (53.8)	58 (60.4)	27 (43.5)	
Yes	73 (46.2)	38 (39.6)	35 (56.5)	

Categorical values are shown as n (%). Continuous variables are shown as mean ± SEs. Elevated alanine aminotransferase (ALT) level was defined as ALT> 30 U/L in men or > 19 U/L in women. BMI: body mass index; ALT: alanine aminotransferase; MELD: model for end-stage liver disease; L3 SMA: lumbar 3rd skeletal muscle areas; L3 SMI: lumbar 3rd skeletal muscle index. ΔSMI/y: the change in the skeletal muscle index per year.

erector spinae, rectus abdominis, transversus abdominis, and external and internal obliques. The L3 skeletal muscle index (SMI, cm^2/ m^2) was calculated by dividing SMA by the square of height (m^2). Sarcopenia was defined in patients with liver disease using the following cut-off values for SMI: <38 cm^2/m^2 for females and <42 cm^2/m^2 for males [20].

To normalize the results, the differences between the first and second CT were calculated for the SMI divided by the number of days between the first and second CT, and finally multiplied by year to calculate the change per year. The change in the skeletal muscle index per year (ΔSMI/y) was calculated as: ΔSMI/y (%) = ([SMI at the second CT scan-SMI at the baseline CT scan]/[SMI at the baseline CT scan]/interval between CT scans (years)) $\times$ 100 % [21]. LSMM was defined as ΔSMI/y < 0.

2.4. Study outcomes

The primary endpoint of our study was defined as the liver-related mortality by August 31, 2023, according to the follow up time of patients' initial admission. Liver-related mortality was defined as death due to any of the following reasons: infectious, oncologic, portal hypertensive, variceal bleeding and bleeding [22,23].

Table 2
Baseline characteristics of patients with liver cirrhosis by LSMM (n = 158).

Variables	Non-LSMM (n = 63)	LSMM (n = 95)	p value	Univariable OR	
				95%CI	P-value
Age (years)	54.6 ± 12.3	58.8 ± 12.5	0.040		
<60	37 (58.7)	48 (50.5)	0.311	1	
≥60	26 (41.3)	47 (49.5)		1.39 (0.73–2.65)	0.312
Male (n,%)	40 (63.5)	56 (58.9)	0.567	1.21 (0.63–2.33)	0.567
BMI (kg/m^2)	23.0 ± 3.7	23.4 ± 3.7	0.469		
<28	58 (92.1)	85 (89.5)	0.587	1	
≥28	5 (7.9)	10 (10.5)		1.36 (0.44–4.2)	0.588
Alcoholic cirrhosis			0.235		
No	38 (60.3)	66 (69.5)		1	
Yes	25 (39.7)	29 (30.5)		0.67 (0.34–1.3)	0.236
Co-morbidities (n, %)					
Hypertension			0.102		
No	47 (74.6)	59 (62.1)		1	
Yes	16 (25.4)	36 (37.9)		1.79 (0.89–3.62)	0.104
Diabetes			0.120		
No	49 (77.8)	63 (66.3)		1	
Yes	14 (22.2)	32 (33.7)		1.78 (0.86–3.69)	0.123
Chronic kidney disease			0.028		
No	62 (98.4)	84 (88.4)		1	
Yes	1 (1.6)	11 (11.6)		8.12 (1.02–64.5)	0.048
Laboratory parameters					
Thrombocyte (× 10^9/L)	113.1 ± 73.4	95.9 ± 49.1	0.079		
ALT (IU/L)	23.0 (17.0, 43.0)	27.0 (20.0, 42.5)	0.337		
<ULN	31 (49.2)	39 (41.1)	0.312	1	
≥ULN	32 (50.8)	56 (58.9)		1.39 (0.73–2.64)	0.313
MELD score	8.9 ± 4.8	9.9 ± 4.5	0.181	1.05 (0.98–1.13)	0.181
Complications (n, %)					
Hepatocellular carcinoma			0.114		
No	52 (82.5)	68 (71.6)		1	
Yes	11 (17.5)	27 (28.4)		1.88 (0.85–4.13)	0.118
Ascites			0.339		
No	28 (44.4)	35 (36.8)		1	
Yes	35 (55.6)	60 (63.2)		1.37 (0.72–2.62)	0.34
Variceal bleeding			0.318		
No	61 (96.8)	88 (92.6)		1	
Yes	2 (3.2)	7 (7.4)		2.43 (0.49–12.08)	0.279
Spontaneous bacterial peritonitis			0.915		
No	54 (85.7)	82 (86.3)		1	
Yes	9 (14.3)	13 (13.7)		0.95 (0.38–2.38)	0.915
Hepatic encephalopathy			0.074		
No	55 (87.3)	72 (75.8)		1	
Yes	8 (12.7)	23 (24.2)		2.2 (0.91–5.28)	0.079
Radiographic analysis					
L3 SMI (cm^2/m^2)	40.8 ± 8.2	41.7 ± 8.9	0.54	1.01 (0.97–1.05)	0.538
Sarcopenia			0.972		
No	34 (54.0)	51 (53.7)		1	
Yes	29 (46.0)	44 (46.3)		1.01 (0.53–1.92)	0.972

LSMM: loss of skeletal muscle mass; OR: odds ratio; CI: confidence interval; Elevated alanine aminotransferase (ALT) level was defined as ALT> 30 U/ L in men or > 19 U/L in women. BMI: body mass index; ALT: alanine aminotransferase; MELD: model for end-stage liver disease; L3 SMI: lumbar 3rd skeletal muscle index.

2.5. Statistical analysis

The normality of the data was evaluated using the Kolmogorov-Smirnov test. The baseline characteristics of the included patients were described as follows: mean ± standard deviation (SD) was used to present normally distributed data, while median [interquartile range (IQR)] was used for non-normally distributed continuous data. Categorical variables were presented as number (%). To identify significant differences between groups, chi-square tests were employed for categorical variables, Mann-Whitney tests were used for non-normally distributed continuous variables, and independent sample T tests were conducted for normally distributed continuous variables.

To identify potential risk factors for LSMM, a multivariate logistic regression analysis was employed. The competing risk model was utilized to examine liver-related mortality. All statistical tests were two-tailed, with a p-value <0.05 considered statistically significant. Statistical analysis was conducted using the R software package (http://www.R-project.org, version 4.1.1, R Foundation for Statistical Computing, Vienna, Austria.).

3. Results

3.1. Baseline characteristics of patients with liver cirrhosis by gender

We conducted a retrospective analysis of 284 patients. Individuals who did not meet the specified criteria were excluded from the study: those with incomplete information (n = 59), those who did not undergo a follow-up CT scan performed at least 6 months after the initial scan (n = 24), those who underwent liver transplantation (n = 5), those with incurable malignancies other than HCC (n = 27), those with severe chronic respiratory or heart diseases (n = 10), and those with nephrotic syndrome (n = 1). Ultimately, the analysis encompassed a group of 158 patients who had been diagnosed with liver cirrhosis. Within this cohort, 96 (60.8 %) were males, with an average age of 57.1 ± 12.6 years, and females were older than males (61.4 ± 11.0 vs. 54.4 ± 12.8, $p < 0.001$). It was observed that a higher percentage of males had alcoholic cirrhosis compared to females (55.2 % vs. 1.6 %, $p < 0.001$). Additionally, males exhibited a greater proportion of ALT levels below the upper limit of normal values and combined with SBP (56.2 % vs. 25.8 % and 18.8 % vs. 6.5 %, respectively, $p < 0.001$). The mean MELD score for the entire study was 9.5 ± 4.6, and 24.1 % were combined with HCC, but no notable variances were observed between these two groups. The radiographic analysis revealed significant differences, while males had a higher SMI (44.1 ± 9.2 vs. 37.1 ± 5.3, $p < 0.001$) and less sarcopenia (39.6 % vs. 56.5 %, $p = 0.038$) compared to females. The median of ΔSMA/y% was −0.9 (IQR: -3.8,1.6) in all patients, however, no significant statistical distinction was observed between the two groups. (Table 1).

3.2. Baseline characteristics of patients with liver cirrhosis by LSMM and univariate analysis of risk factors

Among the total patients, 95 (60.1 %) patients were diagnosed with LSMM. The group of patients with LSMM exhibited older age (58.8 ± 12.5 vs. 54.6 ± 12.3, $p = 0.001$) and displayed a higher prevalence of CKD (11.6 % vs. 1.6 %, $p = 0.028$) (Table 2). Fig. 1 depicted the CT images used to evaluate the body composition of a patient who initially had liver cirrhosis but later developed sarcopenia during the follow-up period. The univariate analysis showed that cirrhotic patients with LSMM had an increased susceptibility to hypertension, diabetes, CKD, HCC and HE compared with non-LSMM patients, however, only CKD had a statistical difference (odds ratio [OR], 8.12; 95 % confidence interval [CI], 1.02–64.5, $p = 0.048$) (Table 2).

3.3. Factors predicting liver-related mortality in patients with cirrhosis

Overall, 61 cirrhotic patients died during the median follow-up of 68.1(IQR, 43.5, 105.0) months, of which 57 patients died of liver-
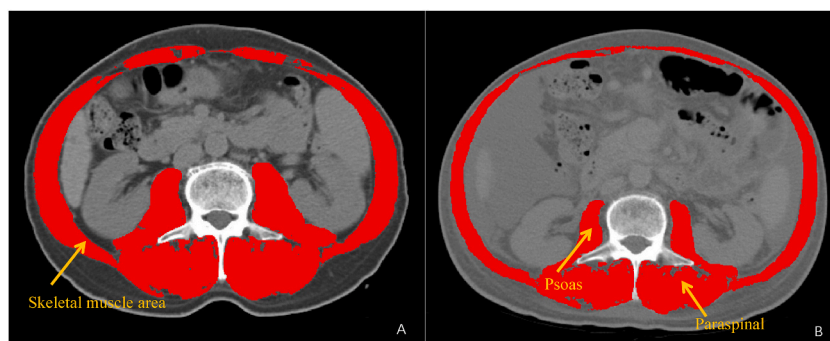

Fig. 1. Computed tomography images of a 60-year-old male. He was diagnosed as cirrhosis caused by chronic infection of hepatitis B virus, who died for acute-on-chronic liver failure and hepatocellular carcinoma about 4 years after baseline. The axial abodominal CT scan (third lumbar vertebra) of the patient without sarcopenia (A) at baseline and with sarcopenia (B) 4 years later are compared (SMA: 133.5 cm^2 vs. 105.8 cm^2; SMI: 49.04 cm^2/m^2 vs. 38.87 cm^2/m^2). Skeletal muscle area is highlighted in red.

related diseases. In univariate analysis, ascites, SBP, HE, MELD score, L3 SMI and LSMM exhibited significant associations with liver-related mortality (Table 3). In multivariate analysis, ascites (hazard ratio [HR], 3.28; 95%CI, 1.68–6.38, $p < 0.001$) and LSMM (HR, 1.86; 95 % CI, 1.01–3.44, $p = 0.047$) were independently associated with liver-related mortality.

Patients without LSMM exhibited a notably superior cumulative survival rate in contrast to those with LSMM (log-rank test, $p = 0.004$) (Fig. 2). Survival rates at 1-, 3-, and 5-years were 96.8 %, 81.0 %, and 65.1 %, respectively, for patients without LSMM, and 97.9 %, 80.0 %, and 56.8 %, respectively, for patients with LSMM.

4. Discussion

Through a retrospective cohort analysis involving regular CT scans, we examined the risk factors and prognostic implications of skeletal muscle depletion over a six-month period in individuals diagnosed with liver cirrhosis, and our findings confirmed that CKD may have a positive correlation with the risk of LSMM, besides ascites and LSMM were found to be independent factors associated with long-term liver-related mortality in cirrhotic patients.

Table 3
Factors predicting liver-related mortality in liver cirrhosis.

Variables	Univariate HR		Multivariate HR	
	95 % CI	p value	95 % CI	p value
Age (years)				
<60	1		1	
≥60	1.59 (0.96,2.63)	0.072	1.08 (0.63–1.87)	0.775
Male (n,%)	1.14 (0.68,1.91)	0.626	1.19 (0.67–2.12)	0.544
BMI (kg/m^2)				
<28	1			
≥28	1.23 (0.58,2.6)	0.584		
Alcoholic cirrhosis				
No	1			
Yes	1.42 (0.85,2.37)	0.175		
Hypertension				
No	1			
Yes	1.25 (0.75,2.09)	0.394		
Diabetes				
No	1			
Yes	1.13 (0.66,1.94)	0.647		
Chronic kidney disease				
No	1		1	
Yes	1.79 (0.77,4.18)	0.176	1.2 (0.5–2.88)	0.691
Hepatocellular carcinoma				
No	1			
Yes	1.4 (0.83,2.38)	0.211		
Ascites				
No	1		1	
Yes	3.88 (2.08,7.24)	<0.001	3.28 (1.68–6.38)	<0.001
Variceal bleeding			1.53 (0.57–4.12)	0.398
No	1			
Yes	2.32 (0.93,5.82)	0.072		
Spontaneous bacterial peritonitis				
No	1		1	
Yes	3.68 (1.91,7.08)	<0.001	1.66 (0.91–3.04)	0.096
Hepatic encephalopathy				
No	1			
Yes	2.76 (1.58,4.81)	<0.001		
Thrombocyte ($\times 10^9$/L)	0.9988 (0.9944,1.0031)	0.574		
ALT(IU/L)				
<ULN	1			
≥ULN	0.6 (0.28,1.26)	0.179		
MELD score	1.07 (1.01,1.14)	0.023	1.04 (0.98–1.11)	0.188
L3 SMI (cm^2/m2)	0.96 (0.93,0.99)	0.012		
LSMM				
No	1		1	
Yes	2.26 (1.28,4.02)	0.005	1.86 (1.01–3.44)	0.047
Sarcopenia				
No	1		1	
Yes	1.58 (0.95,2.61)	0.077	1.57 (0.91–2.72)	0.108

The multivariate model was adjusted for age, gender, chronic kidney disease, ascites, variceal bleeding, hepatic encephalopathy, MELD and LSMM. LSMM: loss of skeletal muscle mass; HR: hazards ratio; CI: confidence interval; Elevated alanine aminotransferase (ALT) level was defined as ALT> 30 U/L in men or > 19 U/L in women. BMI: body mass index; ALT: alanine aminotransferase; MELD: model for end-stage liver disease; L3 SMI: lumbar 3rd skeletal muscle index.
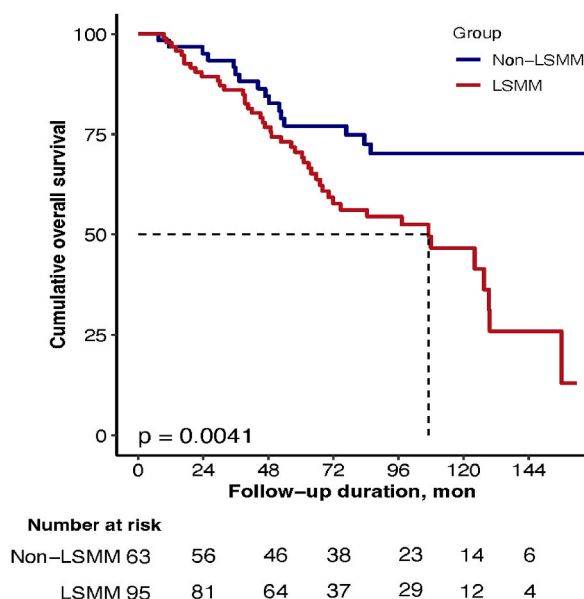
Fig. 2. Survival rates of cirrhotic patients with or without LSMM. LSMM: loss of skeletal muscle mass.

According to our analysis, only CKD was a risk factor for LSMM in individuals with liver cirrhosis (OR, 8.12; 95%CI, 1.02–64.5, $p = 0.048$). CKD is often referred to as an "accelerated aging" model, implying that diminished skeletal muscle strength, the decline in lean mass, and impaired physical performance align with patient-centered outcomes associated with aging, such as limitations in mobility, disability, and mortality, as observed within the general population [24,25]. Among a cohort of 287 non-dialysis CKD patients, Pereira et al. [26] found the prevalence of sarcopenia ranged from 5.9 % to 9.8 %, and dialysis patients showed a slightly higher prevalence of sarcopenia. In a study by Souza et al. [27] comprising 100 patients, the prevalence of sarcopenia was found to be 11.9 % based on the European Working Group on Sarcopenia in Older People (EWGSOP) criteria and 28.7 % based on the criteria set by the Foundation for the National Institutes of Health. With the progression of CKD stages, there is a tendency for the frequency of sarcopenia to rise. In another investigation conducted by Kim et al. [28] on 95 hemodialysis patients, the occurrence of sarcopenia was found to be 37 % in men and 29.3 % in women. The primary mechanisms underlying sarcopenia in individuals with CKD are centered on the depletion of muscular tissue. This presents a challenging paradox, as it remains unclear whether decreased physical activity contributes to muscle depletion or if muscle depletion leads to reduced activity. Despite the elusive underlying cause, the decrease in muscle mass observed in CKD can be attributed to an imbalanced protein homeostasis, leading to increased muscle breakdown and reduced muscle synthesis [24,26,28].

Many previous investigations have demonstrated that SMI and sarcopenia have independent associations with prognosis in patients with cirrhosis, encompassing survival and the development of complications related to cirrhosis [29–31]. The precise mechanism by which sarcopenia leads to a poorer prognosis remains unclear [32]. Nevertheless, skeletal muscle serves as an organ that releases a variety of peptides and cytokines. The onset of sarcopenia leads to hormonal and biochemical alterations, resulting in elevated levels of circulating endotoxins. Consequently, there is an increased susceptibility to infection due to compromised immune function and a higher risk of HE [33]. Hence, many endeavors have been undertaken to ameliorate sarcopenia among individuals suffering from cirrhosis. However, this study differs from some of the prior studies described above as we did not find the association of sarcopenia with liver-related mortality (HR:1.57, 95%CI, 0.91–2.72, $p = 0.108$). A retrospective study including 149 patients with liver cirrhosis by Hanai T et al. [34] found that in the multivariate analysis sarcopenia did not emerge as a predictive factor (HR:1.71, 95%CI, 0.86–3.62, $p = 0.13$). A meta-analysis exploring the influence of sarcopenia on outcomes among cirrhotic patients revealed a higher mortality risk associated with sarcopenia in individuals with ALD compared to those without ALD (pooled adjusted HR 2.67, 95 % CI 1.60–4.47 and 2.09, 95 % CI 1.34–3.26, respectively) [29]. The divergence of our findings from other studies may be attributed to the limited participant size and a relatively small proportion of alcohol-related cirrhotic patients.

Individuals with cirrhosis frequently encounter body composition alterations, which manifest as a decline in skeletal muscle mass [32,35]. The overall population experiences a progressive decline in skeletal muscle mass that typically initiates between the ages of 30 and 40 [36,37]. The decrease in muscle mass associated with aging is estimated to be around 0.3%–0.8 % annually until the age of 60–70, at which point it escalates to 1.5 % per year [37]. Our findings demonstrated that patients with cirrhosis exhibited a yearly decrease in skeletal muscle mass of 0.9 %, which only displayed a slightly higher rate when compared to the general population. In addition, Hanai et al. [34] and Jeong et al. [32] have highlighted the independent impact of skeletal muscle mass change on the prognosis of patients with cirrhosis, regardless of the MELD or CP score. Similarly, our study also indicated a significant correlation between LSMM and liver-related mortality in cirrhotic individuals, regardless of the presence of sarcopenia. When evaluating the prognosis of cirrhotic patients with a follow-up period exceeding 6 months, which allowed for adequate muscle mass loss, multivariate

analysis indicated a significant involvement of LSMM in the mortality of these patients (HR = 1.86, 95 % CI = 1.01–3.44, p = 0.047), consistent with findings reported by Hanai T, et, al. [34] and Jeong JY, et, al. [32], although the threshold for defining LSMM is different (LSMM were defined as $\Delta SMA/y < -3.1\,\%$ and $\Delta SMA/y < -2.4\,\%$, respectively).Therefore, the evaluation of LSMM through the assessment of $\Delta SMA/y$ proves to be a valuable predictor for the prognosis of individuals diagnosed with cirrhosis.

This study encountered some limitations. Firstly, it consisted of a retrospective analysis that took place exclusively at a solitary medical center, involving a constrained patient population. Secondly, our investigation relied on cross-sectional CT scans to estimate the skeletal muscle area, which is associated with drawbacks including high expenses and radiation exposure. Additional investigation is necessary to further explore the potential benefits of alternative techniques, including dual-energy X-ray absorptiometry, bioelectrical impedance analysis, and anthropometry, in predicting the prognosis of cirrhotic patients by assessing skeletal muscle mass. Lastly, this study solely focused on assessing sarcopenia based on muscle mass and did not consider muscle function. Future studies should encompass the measurement of physical activity and encompass a wider range of bodily functions.

To summarize, the assessment of LSMM proves valuable in predicting liver-related mortality in individuals with cirrhosis. Focusing on the management of skeletal muscle could potentially enhance the prognosis of cirrhotic patients. Furthermore, additional comprehensive investigations are required to validate this potential benefit.

CRediT authorship contribution statement

Jiarui Zheng: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Shuo Yang:** Software, Methodology, Data curation. **Wenhui Ren:** Methodology. **Juan Zhong:** Investigation. **Xin Liu:** Resources. **Rui Han:** Resources. **Tingyang Wei:** Resources. **Changjie Tie:** Resources. **Yuteng Yang:** Resources. **Chengwu Hong:** Resources. **Bo Feng:** Writing – review & editing, Validation, Supervision. **Rui Huang:** Writing – review & editing, Visualization, Validation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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