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Research article

Meld-sarcopenia score and skeletal muscle density predicts short-term readmission of patients with hepatic encephalopathy

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ABSTRACT

Purpose: To investigate whether the quality of skeletal muscle mass could predict short-term readmission in patients with hepatic encephalopathy (HE).

Method: Patients with HE were enrolled from 2018 to 2022. Sarcopenia and myosteatosis were defined using the L3 skeletal muscle index (SMI) and skeletal muscle density (SMD) obtained from CT imaging. MELD-Sarcopenia score was calculated. Multivariable analysis and multiple linear regression were applied to identify predictors of 30-day readmission and length of hospitalization.

Results: 123 patients with HE were included. 55 (44.7%) and 87 (70.7%) patients were identified with sarcopenia and myosteatosis, respectively. Patients with sarcopenia exhibited a higher prevalence of myosteatosis, lower SMI and SMD ($p < 0.05$). Patients with myosteatosis were older, had a lower body mass index, a higher neutrophil-to-lymphocyte ratio and MELD-sarcopenia scores ($p < 0.05$). 10 (8.1%) patients were readmitted within 30 days. The readmitted group had a higher MELD-sarcopenia score (25.0 ± 6.6 vs. 19.5 ± 7.8, $p = 0.034$) and lower L3 SMD (28.3 ± 5.9 vs. 33.8 ± 6.9, $p = 0.015$). In the multivariable analysis, MELD-sarcopenia score (95% CI 1.388 [1.074–1.793], $p = 0.012$) and SMD (95% CI 0.778 [0.610–0.991], $p = 0.042$) were found to be significantly associated with the 30-day readmission of patients with HE. Age ($p = 0.028$), alcohol liver disease ($p = 0.025$), and hypertension ($p = 0.003$) were associated with the length of hospitalization for patients with HE.

Conclusions: The MELD-sarcopenia score and SMD were identified as predictive factors for short-term readmission in patients diagnosed as HE.

1. Introduction

Sarcopenia and myosteatosis are conditions that reflect the quality of skeletal muscle mass and are closely associated with patients suffering from various severe wasting disease, including cancer, diabetes, trauma, sepsis, lung disease, renal failure, heart failure and end-stage liver disease [1,2]. Patients with cirrhosis often experience changes in their body composition, such as the development of sarcopenia and myosteatosis [3]. Sarcopenia is a syndrome characterized by the progressive and generalized loss of skeletal muscle mass, strength and function. It represents a potentially life-threatening extrahepatic manifestation of cirrhosis [4]. In cirrhotic patients, sarcopenia is commonly attributed to factors such as protopathy, low physical activity, and poor nutrition [5]. Myosteatosis is now recognized as a physiologically relevant fat depot that may play a pivotal role in the risk of metabolic abnormalities [6]. Myosteatosis has been linked to insulin resistance and type 2 diabetes mellitus, influencing lipid and lipoprotein levels, as well as being associated with biomarkers of inflammation in middle-aged and older adults [6]. The underlying mechanisms require further elucidation in future research. Researchers have found that the presence of sarcopenia and myosteatosis is independently associated with overt hepatic encephalopathy (HE) and a higher long-term mortality risk in patients with

Abbreviations: HE, hepatic encephalopathy; BMI, body mass index; HCC, hepatocellular carcinoma; SBP, spontaneous bacterial peritonitis; NLR, neutrophil-to-lymphocyte ratio; MELD-sarcopenia score, the Model for End-Stage Liver Disease-sarcopenia score; SMI, skeletal muscle index; SMD, skeletal muscle density; SMA, skeletal muscle areas.

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cirrhosis [7].

HE is a known complication of deteriorate cirrhosis that leads to poor outcome and reduced quality of life. It has been reported that HE is the most common cause of 30- and 90-day readmissions, accounting for 20.7% and 30.1% respectively [8], and it is also associated with increased mortality rates [9]. Readmissions of patients with HE imposes a substantial economic burden on both patients themselves and the healthcare system. In the United States, the economic cost burden of HE-related hospitalizations is estimated to be between $4.67 and $7.24 billion annually, with individual inpatient costs ranging from $46,000 to $63,000 [10]. Several studies have shown that assessing the quality of muscle mass can server as an efficient biomarker for prognosis in patients with cancer, outcomes in cirrhotic patients hospitalized for decompensation, and as a prognostic factor for postoperative complications, length of hospital stay, readmissions, and mortality [2,11–13].

Although sarcopenia and myosteatosis are associated with nutritional status and quality of life in patients with cirrhosis, there is limited research focusing on the predictive value of sarcopenia and myosteatosis in the readmission rates of patients with HE. Therefore, the aim of this retrospective study was to investigate whether the quality of muscle mass could predict the short-term readmission in patients with HE.

2. Material and methods

2.1. Data source

Patients who were admitted to our hospital between January 2018 and December 2022 and diagnosed with HE based on the following ICD-9 codes: 570.X, 572.2, 348.3, 348.31, 348.39, and 291.2, were eligible in this study. The inclusion criteria consisted of the following: a) patients aged 18 years or older; b) availability of complete patients' information; c) patients' CT imagines at the third lumbar vertebra were obtained and available to analyze; d) patients with 30-day readmission were defined as patients' first liver-related readmission within 30 days following the patients' initial admission; e) liver-related readmission was defined as readmission due to any of the following reasons: HE, volume-related complications (ascites, edema, hepatic hydrothorax and spontaneous bacterial peritonitis [SBP]), hepatocellular carcinoma (HCC) and variceal bleeding. Patients were excluded from the study if they met any of the following exclusion criteria: a) incomplete patients' information; b) patients who died during the follow-up period. The study was conducted in accordance with the ethical guidelines outlined in the 1975 Declaration of Helsinki (6th revision, 2008) and received approval from the ethics committee of Peking University People's Hospital (No. 2022PHB251-01). As the study is a retrospective study, informed consent was waived.

2.2. Baseline characteristics

We extracted patients' hospitalization information from the electronic medical records of our hospital. The following patients' characteristics were collected: age, sex, height, body mass index (BMI), the grade of HE, underlying liver disease, co-morbidities (hypertension, diabetes, chronic kidney disease), complications (HCC, ascites, variceal bleeding, SBP). The diagnosis and grade of HE according to the guidelines published in 2014 [14]. According to the guideline, Grade 1 is described as a slight lack of awareness, shortened attention span, impairment of addition or subtraction, or altered sleep rhythm. Grade 2 is characterized by lethargy or apathy, disorientation with respect to time, obvious personality changes, inappropriate behavior, dyspraxia, and asterixis. Grade 3 is described as somnolence leading to semistupor, responsiveness to stimuli, confusion, severe disorientation, and bizarre behavior. Grade 4 is characterized by coma. Laboratory parameters (albumin, serum ammonia and neutrophil-to-lymphocyte ratio [NLR]), MELD-sarcopenia score, and radiographic analysis (L3 skeletal muscle index [SMI], L3 skeletal muscle density [SMD], myosteatosis) were also collected.

2.3. Analysis of CT imaging parameters

The CT imaging was performed using the Philips 256-slice iCT scanner from Holland (tube voltage 120 kV, tube current 160mAs, slice thickness 5 mm, pitch 0.980:1) and the GE Lightspeed VCT with 256 layers from the USA (tube voltage 120 kV, tube current 150mAs, slice thickness 5 mm, pitch 0.992:1). All images were reviewed by one well trained and experienced radiologist who had more than 10 years of experience in abdoman CT study interpretation. The radiologist was blinded to the clinical information. Subsequently, the CT images were analyzed utilizing SliceOmatic V5.0 software (Tomovision, Montreal, Canada). This software enables precise tissue demarcation by utilizing established Hounsfield unit (HU) thresholds that have been previously reported[3,4]. To measure skeletal muscle areas (SMA), including the psoas, quadratus lumborum, erector spinae, transversus abdominis, rectus abdominis, and external and internal obliques, attenuation values ranging from −29 to 150 HU were employed at the level of the third lumbar vertebra. The SMI was calculated by dividing the SMA by the square of the patient's height (m^2). The mean SMD was determined as the average density of the skeletal muscle area at the third lumbar vertebra. Sarcopenia was defined in patients with end-stage liver disease as L3 SMI < 39 cm^2/m^2 for women and < 50 cm^2/m^2 for men [4,15]. Myosteatosis was defined based on the mean SMD using cut-off values of < 41 HU in patients with a BMI < 25 kg/m^2 and < 33 HU in patients with a BMI ≥ 25 kg/m^2 [16]. The Model for End-Stage Liver Disease-sarcopenia (MELD-Sarcopenia) score was calculated as follows: MELD score + 10.35 × Sarcopenia [17]. MELD score was calculated with a standard formula: MELD = 3.78 × log [serum bilirubin (mg/dL)] + 11.2 × log [international standardized ratio] + 9.57 × log [serum creatinine] + 6.43 [18].

2.4. Study outcomes

The primary endpoint of our study was defined as the first liver-related readmission within 30 days following the patients' initial admission. We made efforts to capture every hospitalization event that occurred between follow-ups in order to identify if patients were readmitted to other hospitals subsequent to their initial liver-related admission at our hospital.

2.5. Statistical analysis

Data analyses were conducted using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA). Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were presented as counts with percentages. For age, BMI, laboratory parameters, MELD-sarcopenia score, and radiographic analysis, a *t*-test was utilized to compare the groups (sarcopenia vs. non-sarcopenia, myosteatosis vs. non-myosteatosis, readmission vs. non-readmission). Chi-square tests were employed for sex, baseline liver disease, co-morbidities, and complications. Univariable and multivariable analysis were performed to identify predictors of 30-day readmission in patients with HE and multiple linear regression analysis was used for predictors of length of hospitalization. Statistical significance was determined at a p value < 0.05.

3. Results

3.1. Baseline characteristics of patients with HE by sarcopenia

148 patients were included. 15 patients were excluded with incomplete clinical or CT information, while 10 patients were excluded with missing information of readmission. A total of 123 patients with HE was included in the study. Among these patients, 88 (71.5%) were males,

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with a mean age of 59.3 ± 10.9 years. Among the patients, 55 (44.7%) had sarcopenia, 87 (70.7%) were identified with myosteatosis, 52 (42.3) patients had both sarcopenia and myosteatosis, and 33 (26.8%) patients had neither sarcopenia nor myosteatosis. Totally, the classification of HE was 93(75.6%) of grade 1, 19(15.4%) of grade 2 and 11(8.9%) of grade 3. Compared to the patients without sarcopenia, those with sarcopenia exhibited fewer males (31 [56.3%] vs. 57 [84.8%], $p = 0.001$), a lower BMI of 21.6 ± 3.0 vs 25.7 ± 3.7 ($p = 0.001$) and a higher MELD-sarcopenia score of 25.4 ± 7.4 vs 16.2 ± 6.1 ($p = 0.000$), a higher NLR of 5.4 ± 8.0 vs 3.1 ± 2.9 ($p = 0.031$). There were a higher proportion of patients with Grade 3 HE in the sarcopenia group (9 [16.4] vs. 2 [2.9%], $p = 0.019$). The age between sarcopenia and non-sarcopenia group had no significant difference. The radiographic analysis revealed significant differences between the two groups. Patients with sarcopenia had a higher prevalence of myosteatosis (52 [94.5%] vs. 35 [51.4%], $p = 0.000$), as well as lower SMI (34.6 ± 3.5 vs. 48.7 ± 7.1, $p = 0.000$) and SMD (31.1 ± 6.8 vs. 35.2 ± 6.6, $p = 0.001$) compared to those without sarcopenia (Table 1). Fig. 1 depicts the CT images utilized to assess the muscularity of patients with HE. In Picture A and B, transverse sections of the abdomen from HE patients with and without sarcopenia are presented, with the muscle mass highlighted in red.

Table 1
Baseline characteristics of patients by sarcopenia.

Characteristics	All patients (n = 123)	Sarcopenia (n = 55)	Non-sarcopenia (n = 68)	*p* value
Age (years)	59.3 ± 10.9	61.0 ± 11.7	57.9 ± 10.1	0.120
Male (n,%)	88 (71.5%)	31(56.3%)	57 (84.8%)	0.001
BMI (kg/m^2)	23.9 ± 4.0	21.6 ± 3.0	25.7 ± 3.7	0.000
Baseline liver disease (n, %)				0.366
Alcohol	57 (46.3%)	23 (41.8%)	34 (50%)	
Non-alcohol	66 (53.7%)	32 (51.6%)	34 (50%)	
Co-morbidities (n, %)				
Hypertension	42 (34.1%)	22 (40%)	20 (29.4%)	0.218
Diabetes	39 (31.7%)	20 (36.3%)	19 (27.9%)	0.318
Chronic kidney disease	16 (13%)	8 (14.5%)	8 (11.8%)	0.649
Complications				
Hepatocellular carcinoma	22 (17.9%)	11 (20%)	11 (16.2%)	0.582
Ascites	98 (79.7%)	48 (87.2%)	50 (73.5%)	0.060
Variceal bleeding	21 (17.1%)	9 (16.3%)	12 (17.6%)	0.851
Spontaneous bacterial peritonitis	4 (3.3%)	1 (1.8%)	3 (4.4%)	0.420
Laboratory parameters				
Albumin(g/L)	32.0 ± 3.8	31.8 ± 4.1	32.2 ± 3.7	0.609
Serum ammonia (μmol/L)	69.2 ± 28.9	71.1 ± 33.4	67.7 ± 24.7	0.515
NLR	4.1 ± 5.9	5.4 ± 8.0	3.1 ± 2.9	0.031
Classification of HE				0.019
Grade 1	93 (75.6)	36 (65.5%)	57 (83.8%)	
Grade 2	19 (15.4%)	10 (18.2%)	9 (13.2%)	
Grade 3	11 (8.9%)	9 (16.4%)	2 (2.9%)	
MELD-sarcopenia score	23.1 ± 8.2	25.4 ± 7.4	16.2 ± 6.1	0.00
Radiographic analysis				
L3 SMI (cm^2/m^2)	42.43 ± 9.1	34.6 ± 3.5	48.7 ± 7.1	0.000
L3 SMD (HU)	33.4 ± 7.0	31.1 ± 6.8	35.2 ± 6.6	0.001
Myosteatosis (n, %)	87 (70.1%)	52 (94.5%)	35 (51.4%)	0.000

BMI: body mass index. Non-alcoholic: viral hepatitis, non-alcoholic steatohepatitis, drug-induced liver injury, et al. NLR: neutrophil-to-lymphocyte ratio. HE: hepatic encephalopathy. MELD: model for end-stage liver disease. L3 SMI: lumbar 3rd skeletal muscle index. L3 SMD: lumbar 3rd Mean skeletal muscle density.

3.2. Baseline characteristics of patients with HE by myosteatosis

Among the total patient population, 87 (70.7%) patients were identified with myosteatosis. Patients with myosteatosis were found to be older (61.3 ± 10.6 vs. 54.4 ± 10.0, $p = 0.001$) and had a lower BMI (23.1 ± 3.7 vs. 25.9 ± 3.9, $p = 0.000$). However, they had higher NLR values (4.8 ± 6.7 vs. 2.4 ± 2.1, $p = 0.024$) and MELD-sarcopenia scores (21.9 ± 7.9 vs. 17.5 ± 7.3, $p = 0.024$) compared to patients without myosteatosis (Table 2). Radiographic analysis revealed significant differences between the two groups, with lower SMI (38.9 ± 6.3 vs. 50.9 ± 9.2, $p = 0.000$) and SMD (30.7 ± 6.0 vs. 39.9 ± 4.5, $p = 0.000$) in patients with myosteatosis compared to those without myosteatosis. Patients with myosteatosis had a higher prevalence of sarcopenia (52 [59.8%] vs. 3 [8.3%], $p = 0.000$). Picture C and D depict transverse sections of the abdomen, illustrating patients without and with myosteatosis in HE. In both images, skeletal muscle area with high radiodensity (33 to 150 HU) is highlighted in red, and low radiodensity muscle (−29 to 32HU) is highlighted in yellow. Intramuscular fat area (-190 to −30 HU) is highlighted in blue.

3.3. Baseline characteristics of patients by 30-day readmission

Table 3 displays the readmission rates within a 30-day timeframe for the patients included in the study. Among the total population, 10 (8.1%) patients were readmitted within during the period. A comparison between the readmitted and non-readmitted groups revealed that the readmitted group had a higher MELD-sarcopenia score (25.0 ± 6.6 vs. 19.5 ± 7.8, $p = 0.034$) and lower L3 SMD (28.3 ± 5.9 vs. 33.8 ± 6.9, $p = 0.015$) compared to the non-readmitted group (Table 3).

3.4. Predictors of 30-day readmission

In the univariable and multivariable analysis (Table 4), both the MELD-sarcopenia score and SMD demonstrated a significant association with 30-day readmission. MELD-sarcopenia score [95% CI 1.388 (1.074–1.793), $p = 0.012$], and SMD [95% CI 0.778(0.610–0.991), $p = 0.042$] were significantly associated with 30-day readmission of patients with HE in the multivariable analysis.

3.5. Predictors of length of hospitalization

Table 5 demonstrated the results of multiple linear regression analysis for predicting the length of hospitalization. Age ($p = 0.028$), alcohol liver disease ($p = 0.025$) and hypertension ($p = 0.003$) were associated with the length of hospitalization of patients with HE.

4. Discussion

Our study uncovered a significant difference in the prevalence rates of sarcopenia/non-sarcopenia and myosteatosis/non-myosteatosis among patients with HE. Patients experiencing sarcopenia and myosteatosis exhibited poorer physical conditions in terms of age, BMI, NLR, MELD-sarcopenia score, and quality of muscle mass compared to those without sarcopenia and myosteatosis. Additionally, we found that the MELD-sarcopenia score and SMD were associated with 30-day readmission rates in patients with HE. These findings provided a foundation for implementing nutritional support and medical care strategies for patients with HE.

Our study identified the MELD-sarcopenia score as a good predictor of short-term readmission in patients with HE. Furthermore, significant differences were observed between patients with sarcopenia and non-sarcopenia, as well as between those with myosteatosis and non-myosteatosis. It is worth noting that the MELD score has been widely

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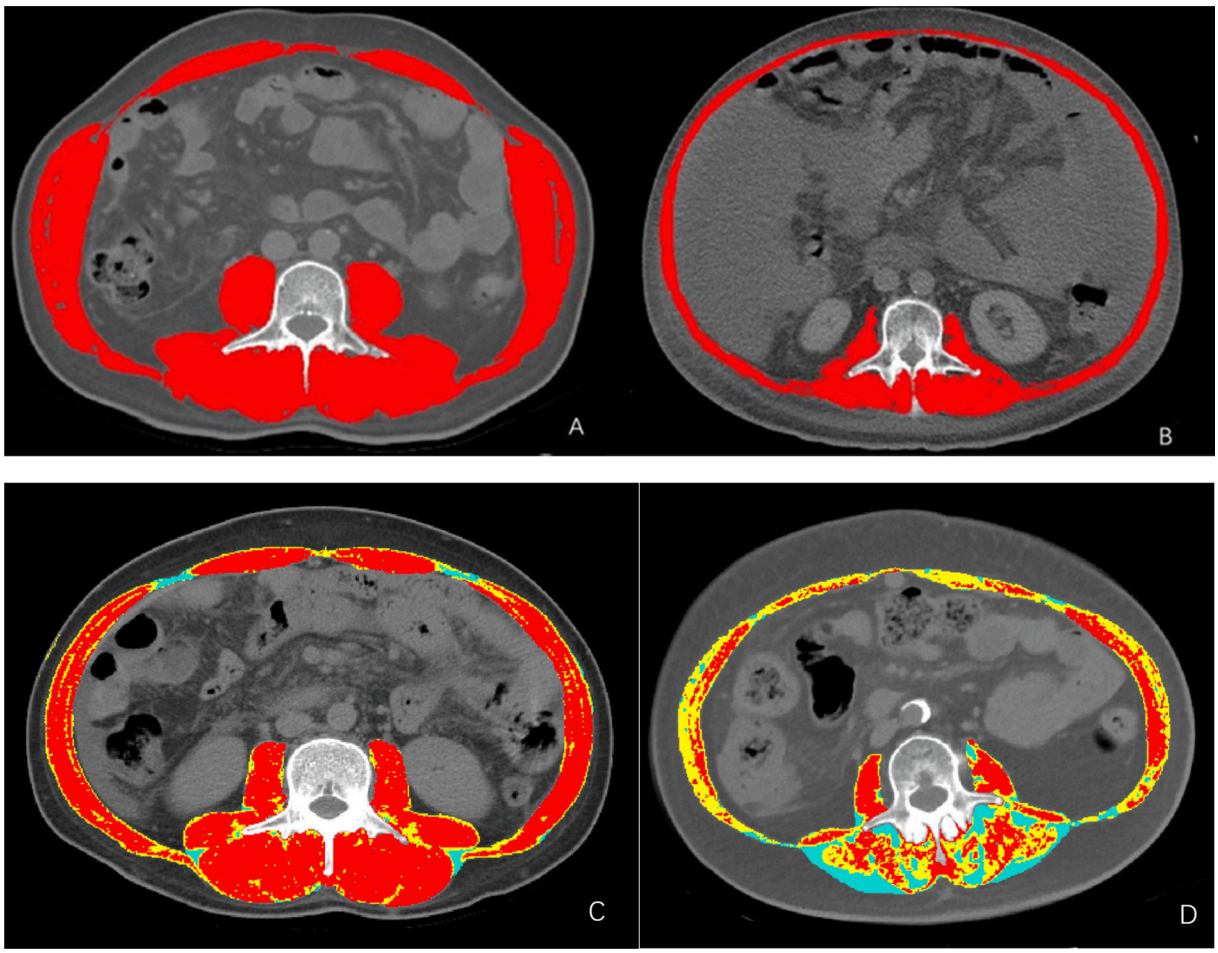

Fig. 1. Computed tomography images used for the muscularity assessment of patients with hepatic encephalopathy. Comparison of two patients without (A) and with (B) sarcopenia. Skeletal muscle area was highlighted in red. Comparison of two patients without (Patient C has normal mean muscle attenuation[45HU]) and with (Patient D has low mean muscle attenuation[26HU]) myosteatosis. Skeletal muscle area with high radiodensity (33 to 150 HU) is highlighted in red, and low radiodensity muscle (−29 to 32HU) is highlighted in yellow. Intramuscular fat area (−190 to −30 HU) is highlighted in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

utilized as a predictive tool for short-term mortality in patients with cirrhosis [19], but some researchers concerning the possible role of nutrition status in the MELDscore to improve accuracy in cirrhotic patients [20]. MELD-sarcopenia score has been found to be a superior predictive model for mortality in patients with HE compared to the MELD score and the albumin bilirubin (ALBI) score [21]. Our study further corroborated these findings by demonstrating the association between the MELD-sarcopenia score and readmission in patients with HE. Other studies have also established a connection between sarcopenia, myosteatosis, and HE [22,23], indicating poor nutrition in patients with cirrhosis. One drawback of the MELD score is its omission of nutritional parameters, resulting in an underestimation of mortality risk in malnourished cirrhotic patients [20]. By incorporating nutrition, a more accurate assessment of HE patients' condition can be achieved. It is worth noting that the validation of the MELD-sarcopenia score in an external cohort remains pending [24]. Barbara et al. concluded that sarcopenia and myosteatosis are independent negative prognostic factors in cirrhotic patients, and these muscle abnormalities often do not coexist in the same patient [20].

SMD is a parameter reflecting the degree of myosteatosis. Patients with myosteatosis are more likely to have sarcopenia and may exhibit lower SMD compared to those without myosteatosis. This could be attributed to the fatty infiltration into skeletal muscle, which reduces muscle attenuation [25]. Myosteatosis is a consequence of multiple mechanisms, including muscle damage, mitochondrial dysfunction, chronic inflammation, and hormone dysregulation [26]. Myosteatosis has been shown to significantly impact muscle function. A study conducted in a cohort of 1330 adults with cirrhosis found that the degree of myosteatosis was positively associated with aging and visceral fat accumulation, while negatively correlated with skeletal muscle mass [27], and the presence of myosteatosis tended to be associated with a poor prognosis. Numerous studies have demonstrated the association of myosteatosis with mortality, minimal and overt HE, and frail phenotype in cirrhotic patients [2,3,28]. In patients with HE, with the accumulation of ammonia and compromised liver capacity to detoxify ammonia, skeletal muscle assumes a compensatory role in ammonia metabolism and clearance. Cirrhotic patients are more susceptible to sarcopenia and myosteatosis, worsening their condition [3,29]. Consequently, myosteatosis could contribute to readmission in patients with HE. Given that myosteatosis and sarcopenia are objective parameters, they have the potential to become valuable tools in prognosticating cirrhosis [3]. Furthermore, minimizing muscle mass loss could be an avenue for improving the condition of HE patients.

Several researches revealed that sarcopenia was a common complication of liver cirrhosis and associated with the development of HE, refractory ascites and pre-transplant mortality [30,31]. Patients with sarcopenia had worse values of MELD-sarcopenia score and increased infection risk as well as reducing quality of life in cirrhosis [31]. Another research concluded that sarcopenia and myosteatosis were associated with elevated NLR [32]. These results were similar with our result:

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Table 2
Baseline characteristics of patients by myosteatosis.

Characteristics	Myosteatosis (n = 87)	Non-myosteatosis (n = 36)	*p* value
Age (years)	61.3 ± 10.6	54.4 ± 10.0	0.001
Male (n,%)	58 (66.7%)	30 (83.3%)	0.062
BMI (kg/m^2)	23.1 ± 3.7	25.9 ± 3.9	0.000
Baseline liver disease (n, %)			0.786
Alcohol	41 (47.1%)	16 (44.4%)	
Non-alcohol	46 (52.9%)	20 (55.6%)	
Co-morbidities (n, %)			
Hypertension	34 (39.1%)	8 (22.2%)	0.073
Diabetes	28 (32.2%)	11 (30.1%)	0.860
Chronic kidney disease	14 (16.1%)	2 (5.6%)	0.114
Complications			
Hepatocellular carcinoma	15 (17.20%)	7 (19.4%)	0.772
Ascites	69 (79.3%)	29 (80.1%)	0.876
Variceal bleeding	14 (16.1%)	7 (19.4%)	0.653
Spontaneous bacterial peritonitis	4 (4.6%)	0 (0)	0.191
Laboratory parameters			
Albumin(g/L)	32.0 ± 3.8	31.9 ± 3.9	0.928
Serum ammonia (μmol/L)	66.3 ± 28.8	76.3 ± 28.2	0.080
NLR	4.8 ± 6.7	2.4 ± 2.1	0.004
Classification of HE			0.936
Grade 1	65 (74.7%)	28 (77.8%)	
Grade 2	14 (16.1%)	5 (13.9%)	
Grade 3	8 (9.2%)	3 (8.3%)	
MELD-sarcopenia score	21.0 ± 7.9	17.5 ± 7.3	0.024
Radiographic analysis			
L3 SMI (cm^2/m^2)	38.9 ± 6.3	50.9 ± 9.2	0.000
L3 SMD (HU)	30.7 ± 6.0	39.9 ± 4.5	0.000
Sarcopenia (n, %)	52 (59.8%)	3 (8.3%)	0.000

BMI: body mass index. Non-alcoholic: viral hepatitis, non-alcoholic steatohepatitis, drug-induced liver injury, et al. NLR: neutrophil-to-lymphocyte ratio. HE: hepatic encephalopathy. MELD: model for end-stage liver disease. L3 SMI: lumbar 3rd skeletal muscle index. L3 SMD: lumbar 3rd Mean skeletal muscle density.

Table 3
Baseline characteristics of patients by 30-day readmission.

Characteristics	Readmission (n = 10)	Non-readmission (n = 113)	*p* value
Age (years)	61.0 ± 11.2	59.1 ± 10.9	0.605
Male (n,%)	9 (90%)	79 (69.9%)	0.177
BMI (kg/m^2)	24.9 ± 5.0	23.8 ± 3.9	0.388
Baseline liver disease (n, %)			0.118
Alcohol	7 (70%)	50 (44.2%)	
Non-alcohol	3 (30%)	63 (55.8%)	
Co-morbidities (n, %)			
Hypertension	6 (60%)	36 (31.8%)	0.072
Diabetes	3 (30%)	36 (31.9%)	0.904
Chronic kidney disease	3 (30%)	13 (11.5%)	0.096
Complications			
Hepatocellular carcinoma	4 (40%)	18 (15.9%)	0.057
Ascites	9 (90%)	89 (78.8%)	0.397
Variceal bleeding	1 (10%)	20 (17.7%)	0.535
Spontaneous bacterial peritonitis	0 (0)	4 (3.5%)	0.545
Laboratory parameters			
Albumin(g/L)	33.8 ± 4.1	31.8 ± 3.8	0.117
Serum ammonia (μmol/L)	72.2 ± 33.1	69.0 ± 28.6	0.736
NLR	3.5 ± 2.6	4.1 ± 6.1	0.730
Classification of HE			0.173
Grade 1	10 (100%)		83 (73.4%)
Grade 2	0 (0)		19 (16.8%)
Grade 3	0 (0)		11 (9.7%)
MELD-sarcopenia score	25.0 ± 6.6	19.5 ± 7.8	0.034
Radiographic analysis			
L3 SMI (cm^2/m^2)	42.5 ± 9.5	42.4 ± 9.1	0.982
L3 SMD (HU)	28.3 ± 5.9	33.8 ± 6.9	0.015
Sarcopenia (n, %)	5 (50%)	50 (44.2%)	0.502
Myosteatosis (n, %)	8 (80%)	79 (69.9%)	0.726

BMI: body mass index. Non-alcoholic: viral hepatitis, non-alcoholic steatohepatitis, drug-induced liver injury, et al. NLR: neutrophil-to-lymphocyte ratio. HE: hepatic encephalopathy. MELD: model for end-stage liver disease. L3 SMI: lumbar 3rd skeletal muscle index. L3 SMD: lumbar 3rd Mean skeletal muscle density.

patients with sarcopenia had higher MELD-sarcopenia score and higher NLR. NLR is a serological marker that reflects the level of inflammation [33]. Early researchers also found advanced age were associated with myosteatosis among patients with cirrhosis at the decompensation phase [2]. The new founding of our study was that we found MELD-sarcopenia score and SMD were associated with 30-day readmission rates in patients with HE. This is an interesting founding. Previous researches reported that the presence of myosteatosis worsened the prognosis of patients with cirrhosis [27]. In addition, myosteatosis was a poor factor associated with the development of HE [23]. HE is a significant complication of cirrhosis, known to be associated with hospital readmission [9]. We can dope out that myosteatosis is associated with hospital readmission in patients with HE. Many researchers reported the relationship between mortality and myosteatosis, sarcopenia as well as HE [17,20,34,35], but in relation to short-term readmission in patients with HE, few studies had been reported. Regarding to the predictive effect in short-term readmission in HE patients, we suspect that the combination of nutrition status and MELD score can better predict the physical condition in HE patients.

NLR is a serological marker that reflects the level of inflammation [33]. It serves as an indicator of the severity and progression of cirrhosis and has been linked to an increased risk of mortality in patients with alcoholic hepatitis and HE [36,37]. In our study, we observed a significant difference in NLR between patients with sarcopenia and those without, as well as between patients with myosteatosis and those without. Interestingly, our findings contrast with another study where no differences in terms of sarcopenia and multiple inflammatory indicators (such as NLR, platelet-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio) were observed between the groups with and without myosteatosis [2]. However, Raila et al. found an association between NLR and sarcopenia as well as myosteatosis in colorectal cancer patients [32]. These inflammatory indicators warrant further investigation in order to elucidate their relationship with skeletal muscle mass.

Regarding the predictors of length of hospitalization, our study revealed that age, alcoholic liver disease, and hypertension were associated with the duration of hospital stay. However, neither myosteatosis nor sarcopenia showed any correlation with the length of hospitalization. Interestingly, a large cohort study involving 678 cirrhosis patients also reported no difference in the length of hospital stay [7]. These findings contradicted the results of Sunil's study [38], which indicated that perioperative myosteatosis was associated with increased length of hospitalization of liver transplant recipients. The disparity in results could potentially be attributed to differences in the study population and the methods employed for measurement.

Our study has several limitations that should be acknowledged. Firstly, the sample size was small, which restricted our ability to fully investigate the long-term readmission rates associated with sarcopenia and myosteatosis in patients with HE. Additionally, due to a low number of deaths within our cohort, we were unable to analyze the relationship between sarcopenia, myosteatosis, and mortality in patients with HE.

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Table 4
Predictors of 30-day readmission in univariable and multivariable logistic regression analysis.

Characteristics	Univariable OR (95 %CI)	*p* value	Multivariable OR (95 %CI)	*p* value
Age (years)	1.016 (0.957–1.079)	0.602	1.1950 (0.988–1.435)	0.067
Male (n,%)	3.873 (0.472–31.781)	0.207		
BMI (kg/m2)	1.073 (0.915–1.257)	0.386	1.529 (0.951–2.459)	0.080
Alcohol liver disease	2.940 (0.723–11.952)	0.132	41.100 (0.623–2709.992)	0.082
Co-morbidities				
Hypertension	3.208 (0.852–12.078)	0.085	0.489 (0.043–5.528)	0.563
Diabetes	0.917 (0.224–3.752)	0.904	16.0.056 (0.837–307.901)	0.065
Chronic kidney disease	3.297 (0.757–14.349)	0.112		
Complications				
Hepatocellular carcinoma	3.519 (0.901–13.733)	0.070	12.993 (0.385–439.008)	0.153
Ascites	2.427 (0.293–20.110)	0.411		
Variceal bleeding	0.517 (0.062–4.312)	0.542		
Spontaneous bacterial peritonitis	0.000	0.999		
Laboratory parameters				
Albumin (g/L)	1.155 (0.964–1.384)	0.118		
Serum ammonia (umol/L)	1.004 (0.982–1.026)	0.734		
NLR	0.974 (0.841–1.129)	0.730		
Classification of HE				
Grade 1	–	1.000		
Grade 2	0.000	0.998		
Grade 3	0.000	0.999		
MELD-sarcopenia score	1.081 (1.003–1.166)	0.041	1.388 (1.074–1.793)	0.012
Radiographic analysis				
L3 SMD (HU)	0.896 (0.817–0.983)	0.020	0.778 (0.610–0.991)	0.042

BMI: body mass index. Non-alcoholic: viral hepatitis, non-alcoholic steatohepatitis, drug-induced liver injury, et al. NLR: neutrophil-to-lymphocyte ratio. HE: hepatic encephalopathy. MELD: model for end-stage liver disease. L3 SMD: lumbar 3rd Mean skeletal muscle density.

Lastly, the lack of unified criteria to define sarcopenia as evident in different approaches reported in literature may have impacted the conclusions drawn from our study[4,13,39]. A multicenter consortium of 5 North American liver transplantation centers had developed a standardized definition of sarcopenia in men and women, that was SMI of $< 50\ cm^2/m^2$ in men and $< 39\ cm^2/m^2$ in women [4]. Another study defined sarcopenia as SMI $< 41\ cm^2/m^2$ for women and $43\ cm^2/m^2$ for men with BMI $< 25\ kg/m^2$ and $53\ cm^2/m^2$ for men with BMI $\geq 25\ kg/m^2$ [13]. There're also defined sarcopenia as SMI $< 40.31\ cm^2/m^2$ for men and $< 30.88\ cm^2/m^2$ for women[39]. In regard to myosteatosis, there're many different parameters to define it, so the different diagnostic criteria will influence our and other researchers' result on sarcopenia and myosteatosis.

5. Conclusions

In summary, our study identified the MELD-sarcopenia score and the presence of myosteatosis as predictors of 30-day readmission in patients with HE. These findings lay the groundwork for the implementation of nutritional support and medical care strategies aimed at improving outcomes for patients with HE.

Table 5
Predictors of length of hospitalization.

Characteristics	*β*	SE	*p* value	*95 %CI*
Age (years)	−0.250	0.112	0.028	−0.472, −0.028
Male (n,%)	2.634	3.058	0.391	−3.430, 8.698
BMI (kg/m^2)	−0.195	0.305	0.525	−0.800, −0.0410
Alcohol liver disease	−6.116	2.682	0.025	−11.434, −0.799
Co-morbidities (n, %)				
Hypertension	7.617	2.476	0.003	2.709, 12.526
Diabetes	−3.141	2.281	0.171	−7.663, 1.381
Chronic kidney disease	4.335	3.392	0.204	−2.391, 11.061
Complications				
Hepatocellular carcinoma	0.476	2.821	0.886	−5.118, 6.069
Ascites	0.323	2.650	0.903	−4.931, 5.577
Variceal bleeding	3.064	2.824	0.280	−2.535, 8.664
Spontaneous bacterial peritonitis	2.533	6.059	0.677	−9.480, 14.545
Laboratory parameters				
Albumin(g/L)	−0.357	0.274	0.195	−0.899, 0.186
Serum ammonia (μmol/L)	−0.039	0.037	0.292	−0.112, 0.034
NLR	−0.053	0.202	0.793	−0.454, 0.348
Classification of HE(1,2,3)	2.178	1.725	0.210	−1.243, 5.598
MELD-sarcopenia score	0.301	0.171	0.081	−0.038, 0.639
Radiographic analysis				
L3 SMD (HU)	0.140	0.179	0.437	−0.215, 0.494

BMI: body mass index. NLR: neutrophil-to-lymphocyte ratio. HE: hepatic encephalopathy. MELD: model for end-stage liver disease. L3 SMD: lumbar 3rd Mean skeletal muscle density.

CRediT authorship contribution statement

Shuo Yang: Writing – original draft, Methodology, Data curation. **Lin Zhang:** Writing – original draft, Investigation, Data curation. **Qian Jin:** Data curation. **Jian Wang:** Data curation. **Danli Ma:** Data curation. **Jie Gao:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Rui Huang:** .

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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